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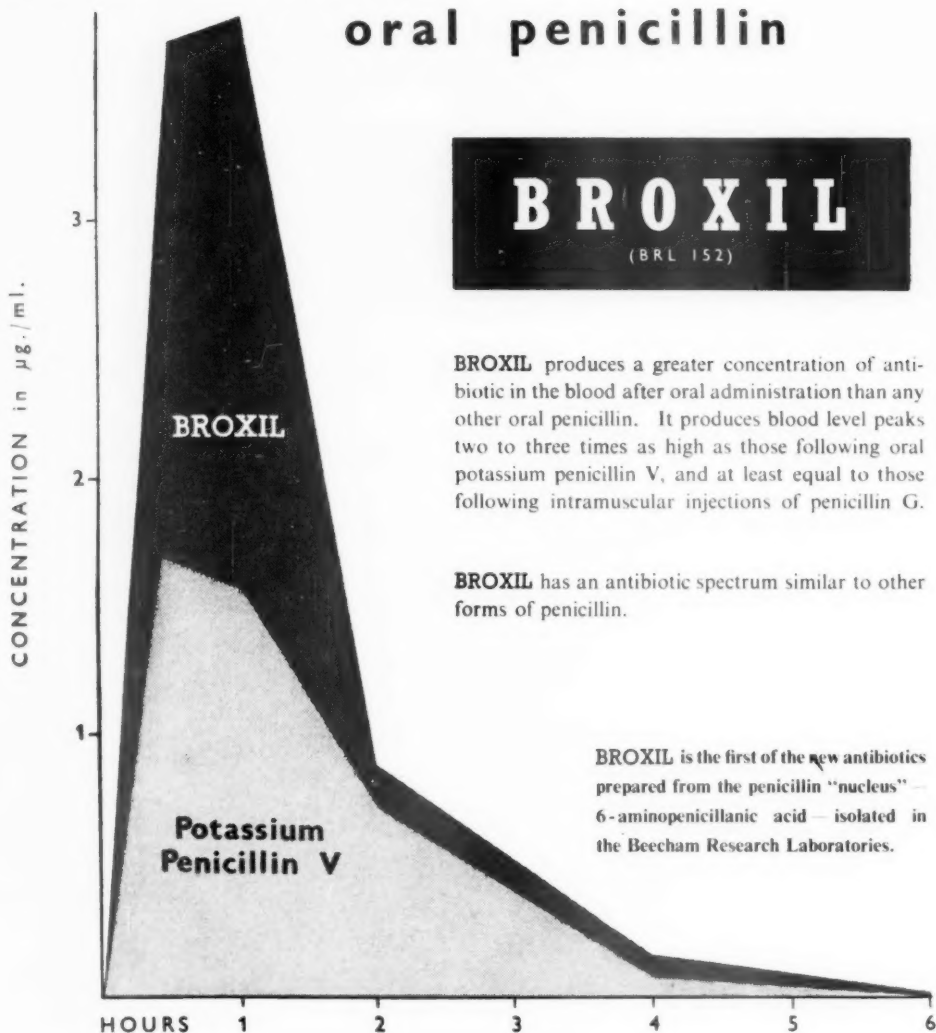
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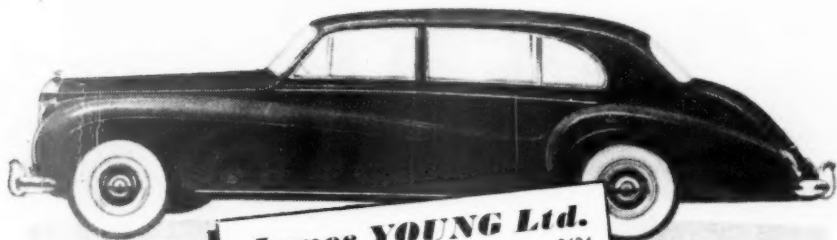
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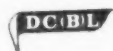
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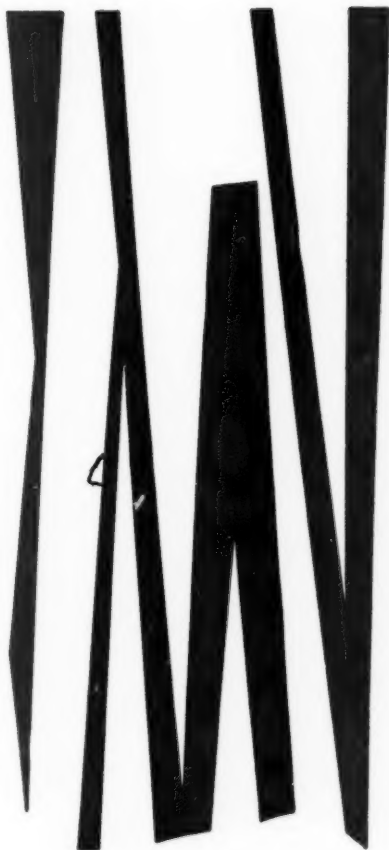
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Reference: *Practitioner*, 1957, 179, 84.

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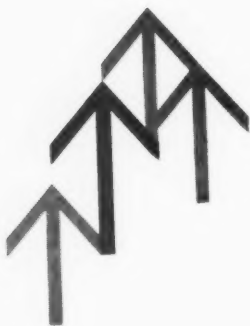
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## Bibliography

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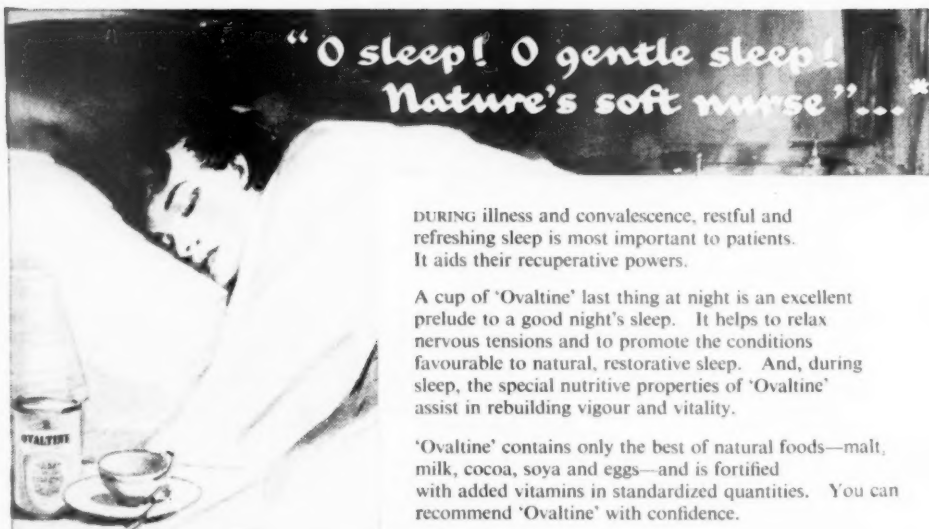
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## Section of Paediatrics

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Meeting  
June 27, 1959

MEETING HELD AT THE ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, BRIGHTON

### EXHIBITS

#### A Survey of Babies Affected by Rhesus Incompatibility during the period April 1, 1951, to March 31, 1959.—JANET GOODALL, M.B., D.C.H.

During this period 226 mothers with Rhesus antibodies were delivered in hospital. Of the 157 affected liveborn infants, 84 needed exchange transfusion within twenty-four hours of birth. 13 neonatal deaths include 2 not related to haemolytic disease in untreated infants. There were 28 stillbirths, in 7 of which maternal toxæmia or hæmorrhage may have been a factor but 5 gave post-mortem evidence of haemolytic disease, the other 2 being macerated.

Induction of labour was performed in 68 cases, 39 at or past term and 22 at 37–39 weeks' gestation, the remaining 7 being for intrauterine death between 28 and 38 weeks' gestation. There were 5 Cæsarean sections at 37–38 weeks. 7 pregnancies were terminated because of previously severely affected infants but not before 37 weeks' gestation.

Treatment was generally given within four hours of birth to any baby of 5½ lb. or less with a positive Coombs' test and to any other baby with a positive Coombs' test and a cord hæmoglobin of less than 15.5 g. % (one left untreated being a case of gross spina bifida). Donor blood was as fresh as possible and exchange was performed on a basis of 60–70 ml. per lb. body weight in most cases.

The series is divided into two periods: in the second period additional help has made it possible to do exchange transfusions at all times and a micro-method for bilirubin estimation had been perfected. The improvement in results is seen in Table I. Retrospective analysis of neonatal deaths (Table II) and stillbirths (Table III) suggests a policy aiming at further improvement.

Of 28 stillbirths 20 occurred from the 35th week of pregnancy onwards. 13 of these were probably avoidable: 7 with a bad past history and rising antibody titre; 2 at term with rising titre; and 4 with unusually high antibody titre. The remaining 7 were considered unavoidable. The fall in stillbirths over the two periods (see Table I) remains unexplained.

*Conclusions and future policy.*—If the father is homozygous Rhesus-positive the severity of haemolytic disease in the infant is likely to increase with maternal parity. Premature induction of labour as advocated by other workers (Kelsall and Vos, 1955; Fisher, 1957) may therefore save life when there is a past history of a severely affected liveborn infant and/or a stillbirth due to haemolytic disease. Remembering the complications of prematurity, the optimal time is probably 35 weeks' gestation onwards with earlier Cæsarean section in specially selected cases. Intrauterine death occurring before 32 weeks' gestation is probably unavoidable.

If the father is heterozygous and there is a significant past history of neonatal death or stillbirth, bilirubin estimations on liquor amnii at 32–35 weeks (Walker, 1957) may indicate an affected fetus. Failing this a marked rise in antibody titre is an indication for premature induction.

Regardless of the past history we consider induction when the antibody titre is unusually high, and no Rhesus-incompatible pregnancy is allowed to go beyond term.

	TABLE I 1951–1955	1956–1959	Total
Mothers with antibodies	101	125	226
Affected liveborn infants	60	97	157
Exchange transfusion within			
twenty-four hours	31	53	84
Affected infants: alive	54	90	144
dead	6	7	13
Stillbirths	21	7	28
Perinatal mortality	27	14	41

TABLE II.—NEONATAL DEATHS
Total 13
2 not due to Rhesus disease (1956–1959).
7 probably avoidable
4 inadequately treated or technical error,
3 very severely affected; not induced.
4 hyaline membrane disease in small infants (3 induced).
1951–55 10% affected liveborn infants died.
1956–59 5.2% affected liveborn infants died (excluding 2 non-Rhesus deaths).

TABLE III.—STILLBIRTHS					
	Gestational age in weeks at death				
	28–32	33–34	35–36	37–41	Total
Total stillbirths	6	2	6	14	28
Previously affected* live-born infant	4	1	3	4	12
Previous neonatal deaths	2	—	3 (1†)	1	6
Previous stillbirths	4	1	2	1‡	8

\*When previous births occurred outside our area "affected" refers to exchange transfusion or neonatal death as reported by the mother.

†Had previous stillbirth also.

‡Probably non-Rhesus death.

We agree with Fisher that each case must be given early and individual consideration by both the obstetrician and paediatrician so that induction, if indicated, can be performed at the optimal time.

My thanks are due to Dr. T. P. Mann for his untiring help in the preparation of this analysis.

#### REFERENCES

- FISHER, O. D. (1957) *Brit. med. J.*, ii, 615.  
 KELSALL, G. A., and VOS, G. H. (1955) *Lancet*, ii, 161.  
 WALKER, A. H. C. (1957) *Brit. med. J.*, ii, 376.

#### A Survey of Congenital Hypertrophic Pyloric Stenosis.—L. W. LAUSTE, F.R.C.S.

Results of Ramstedt's operation from 1949 to 1958 at the Children's Hospital were reviewed. There were 135 operations with 3 deaths (all in 1949). Local anaesthesia (procaine 0.5%) was used in 117 cases, and general ether anaesthesia in 18. The operative complications, post-operative course and treatment were given as well as figures for the average stay in hospital. The tendency is to standardization and simplification of treatment with early discharge.

#### A Study of Cross-infection in The Children's Hospital.—JEAN CREE, M.B., and TREVOR P. MANN, M.D.

Since the beginning of 1956 an attempt has been made to keep a day-to-day record in the medical and surgical wards (excluding the E.N.T. Department) of any infection arising during the patients' hospital stay. Bacteriological evidence of cross-infection was also sought, especially among infants.

Of the 5,201 children admitted in the three-year period under review 422 showed evidence of cross-infection, an overall incidence of 8% (7% clinical). It is of interest that Watkins and Lewis-Faning (1949) in their cross-infection survey ten years ago in 26 children's wards in 14 hospitals of Great Britain arrived at the same figure (7.1%) on a clinical basis. The contrasting patterns of cross-infection in infants and older children were considered. In those under 2 years symptomless *Esch. coli* infection and coliform diarrhoea predominated and represented almost 40% of the cross-infection. In older children upper respiratory infections were considerable, representing over 40% of all cross-infections.

The average yearly expenditure on drugs for both clinical and bacteriological cross-infection was £40, approximately 1% of the total in-patient drug bill.

#### REFERENCE

- WATKINS, A. G., and LEWIS-FANING, E. (1949) *Brit. med. J.*, ii, 616.

The following exhibits were also shown:

#### (1) Radiographic Exhibit. (2) Diagnostic Radiological Quiz.—Dr. J. RUBIN.

Plastic Surgery Exhibit.—Mr. H. ELLIOTT BLAKE.

Photographic Exhibit.—Mr. T. HIGGINS.

Neonatal Cold Injury.—Dr. TREVOR P. MANN.

Infantile Cardiomegaly: the Infantile Type of Endocardial Fibroelastosis.—Dr. R. I. K. ELLIOTT.

#### Clinico-pathological Exhibits

Neonatal Coronary Thrombosis.—TREVOR P. MANN, M.D., and R. I. K. ELLIOTT, D.M.

Female, born 8.1.56. Died aged 4 days.

*Clinical picture.*—Blue asphyxia at birth; cord tight around the neck. Air passages cleared; nasal oxygen; intramuscular Coramine. One hour after birth condition satisfactory. Behaved normally for next seventeen hours.

9.1.56: Vomited altered blood twice. Temperature 91° F. in the morning but 100° F. by evening. Intramuscular streptomycin commenced.

10.1.56: Temperature 99–100° F. Colour poor; in incubator with compressed air. Taking fluid well. Passing urine and meconium.

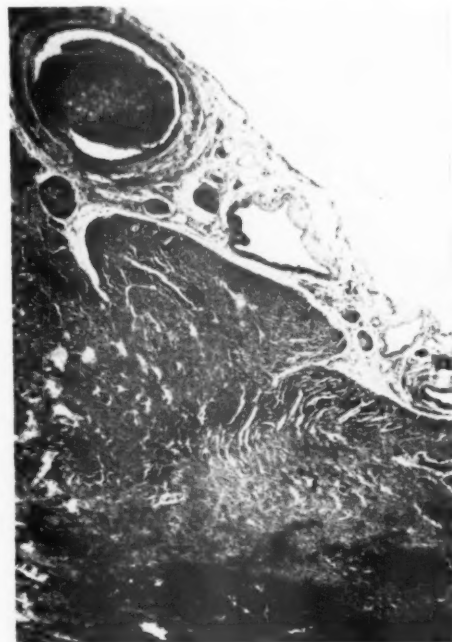


FIG. 1.—Neonatal coronary thrombosis: above, the thrombosed artery; below, infarcted and haemorrhagic myocardium ( $\times 25$ ).

12.1.56: Colour poor; oxygen required. Temperature fell, breathing became distressed, abdomen distended and legs oedematous. Died five hours later.

**Autopsy.**—Lungs expanded, with a few basal hæmorrhagic patches. Heart weighed 23 grams and showed a large ecchymotic patch on the posterior wall of the left ventricle with necrosis of the muscle beneath and a small area of endocardial thrombosis near the apex. Hæmorrhagic streaks were present alongside the coronary arteries.

**Histology.**—Extensive necrosis of the muscle of

the left ventricle with thrombosis of the circumflex and descending branches of the left coronary artery.

The following clinico-pathological exhibits were also shown:

(1) **Suprasellar Astrocytoma ? Infundibuloma.** (2) **Pinealoma.**—Dr. W. MESTITZ, Mr. F. L. DAVIES and Dr. R. I. K. ELLIOTT.

(1) **Reticulum Cell Medullary Reticulosis.** (2) **? Hermaphrodite.**—Dr. TREVOR P. MANN and Dr. R. I. K. ELLIOTT.

**Reticulum Cell Medullary Reticulosis.**—Dr. W. MESTITZ and Dr. R. I. K. ELLIOTT.

## PAPERS

### Experimental Barrier Nursing Techniques in a Cubicled Gastro-Enteritis Unit

By M. GIBSON, R.S.C.N., and TREVOR P. MANN, M.D.

Brighton

When the new cubicled Gastro-Enteritis Unit was opened in July 1958 new nursing techniques were introduced with the object of minimizing cross-infection. On admission the number of cases with bowel pathogens was proportionately the same as in the old uncubiced ward (Table I).

TABLE I

Total incidence of cross-infection in old uncubiced ward (30½ months)	13.8%
50 incidents	
362 cases at risk	
Incidence of cross-infection with bowel organisms in old uncubiced ward (30½ months)	11%
41 incidents	
362 cases at risk	
63 children had bowel pathogens at time of admission	
Total incidence of cross-infection in new cubicled unit (1 year)	5%
8 incidents (involving 6 cases)	
161 cases at risk	
Incidence of cross-infection with bowel organisms in new cubicled unit (1 year)	1.2%
2 incidents	
161 cases at risk	
28 children had bowel pathogens at time of admission	

Neomycin suppression of coliform infections, a common practice in the old ward, was not used although the drug was given occasionally when clinically indicated.

During the first year 8 minor incidents of cross-infection<sup>1</sup> were detected in 6 children, only 2 of these affecting the bowel. Faecal swabs are examined daily by the Public Health Laboratory, Brighton, for specific types of *Esch. coli*.

<sup>1</sup>An infection arising during the course of another illness for which the patient was originally admitted to hospital (Watkins and Lewis-Fanning, 1949).

The nursing techniques on trial in the new Unit have proved to be time-saving and appear to be effective in minimizing cross-infection.

## REFERENCE

WATKINS, A. G., and LEWIS-FANNING, E. (1949) *Brit. med. J.*, ii, 616.

## TECHNIQUES

Feeds warmed in kitchen then taken into cubicle (bottle in stainless steel mug on stainless steel tray). Napkins and clean linen taken in at same time.

### In Cubicle

Feed tray is put on Formica-covered window shelf. The teat is covered by a paper cap which has been put on before terminal heat treatment of feeds.

Nurse puts on gown and prepares to change baby. When soiled napkin is ready for removal foot buzzer is operated by nurse.

Large non-porous paper bag (open) in a saucepan container is brought in by orderly. Soiled soluble napkin put into bag by nurse, taking care NOT to touch the outside of bag. Paper bag then closed over napkin by orderly—outside of bag only being touched.

Container taken straight to incinerator and contents burnt. Container put into sterilizer and boiled for three minutes.

If requested, calico bag for soiled linen is taken into cubicle. The bag is held open by orderly and soiled linen is put in by nurse—then bag is tied up in cubicle by orderly prior to taking it to the sluice room where it is put into a large canvas bag ready for removal to laundry. No linen is "treated" on the ward.

Orderly washes her hands in sluice room between each call.

*During Feeding*

Nurse's clothing is protected by a small mackintosh and terry towelling napkin whenever she has baby on her lap.

*After Feeds*

All feed utensils are washed under tap in cubicle sink, then put into plastic binette which contains Savlon 1:200—fully immersed for an hour—then removed to kitchen for boiling—bottles cleaned with brush and sent for autoclaving.

Nurse removes her gown, washes her hands and comes out of cubicle to hand-drier installed in the corridor. All doors swing both ways and are not touched by hand.

*Technique for Putting on and Taking Off Gowns*

All gowns are kept on coat-hangers and hung on hooks, spaced so that gowns do not touch each other or the furniture. Gown is put on by holding the coat-hanger—this being removed when arms are put into gown, care being taken that outside of gown does not touch dress.

All gowns cover dresses completely. Tapes at the waist are crossed over and tied in front to ensure this. When gown is removed, waist tapes are untied—Hibitane cream is rubbed into hands (from hand-cream dispenser fixed to wall). Tape at neck of gown is then untied and gown is loosened on shoulders to enable it to be removed easily. Hibitane cream is again rubbed into hands and exposed parts of arms. Hanger is slipped into shoulders of gown which is

removed on to hanger, again care being taken not to allow gown to touch dress.

*Cubicle Preparation for Fumigation*

Every cubicle is fumigated after discharge of baby. All bed linen, clothes, towels, &c., are sent to laundry as previously described.

Mattresses, pillows and mackintoshes are left in cubicle.

Locker drawer and cupboard are opened—all equipment is disconnected if possible and spread out.

Cubicle is fumigated by Public Health Authority with Microsol formalin spray.

Just before fumigation a portable door with peripheral sponge rubber seal is fixed on the outside of the cubicle door and left for at least four hours after fumigation.

*Clothing*

Cubicle temperatures average 74° F.

All bed clothing and clothes worn by babies are cotton and can be boiled—minimum of clothing used.

Nurses change from uniform into thin cotton dresses while working in unit.

*Ultra-violet Lamps*

Six ultra-violet lamps are fixed to walls at intervals down corridor and one in treatment room. (Lamps are Phillips Electrical Ltd., A.7002, germicidal fitting.)

Each cubicle contains its own: Auriscope, stethoscope, scales and weights, small scissors, tape measure, pulsometer, ball-point pen, intake and output charts, clinical thermometer, cloths for cleaning, nail brush, wall thermometer, chair.

## Sclerema

By R. I. K. ELLIOTT, M.A., D.M.

Brighton

THE term "scléreme" was introduced by Chaussier in 1815 to describe a form of hardening of the subcutaneous tissues in newborn infants. Chaussier, according to the Dictionnaire Encyclopédique des Science Médicales (1874), was a first-rate scientist, but a muddling lecturer. One may say much the same for the term he originated; it was a good term and very popular, but there is much uncertainty, nowadays, about its meaning. In fact, its very popularity has been its downfall; indiscriminate usage has debased it to the point where it can only be sent to join Bright's disease and Banti's syndrome in limbo.

The purpose of this paper is first to define the three distinct neonatal conditions which were all called sclerema neonatorum; second to trace the historical developments which led to the present confusion—a fascinating story; and third to comment on hardening of the skin and subcutaneous fat in the newborn—a subject where, unfortunately, science is still locked in battle with mythology.

The first type of sclerema neonatorum is also known as subcutaneous fat necrosis. The clinical picture is a familiar one; circumscribed plaques and nodules of hard, discoloured skin, usually over buttocks, shoulders, or cheeks, occurring in an infant otherwise well. In spite of their forbidding appearance, the lesions resolve without treatment, and leave no scar. Some areas become fluctuant, and from these aspiration yields sterile material resembling pus. This, or any other surgical intervention is better avoided because secondary infection may convert an innocuous lesion into a disfiguring one. The histological picture is one of fat necrosis with the usual foreign body giant cell reaction at the periphery. This lesion is not confined to the neonatal period, though it is commonest then; it may occur at any age.

The second type of sclerema I will call "pre-agonal induration." It is the condition which Denman and Underwood (Underwood, 1784) described as "skin-bound". This is a peculiar

alteration in texture of the skin and subcutaneous tissues which appears in the terminal stages of other diseases such as congenital cardiac defect or gastroenteritis. It is a hardening which is usually first perceptible in the legs and then spreads upwards to involve the entire body. The affected skin is pale and cool; it has lost the resilience of normal flesh, and cannot be made to pit on pressure. The diameter of an affected

this lesion develops. No cellular infiltration accompanies the change.

The third type of sclerema is that curious condition, encountered only during cold weather, called neonatal cold injury (Mann, 1955; Mann and Elliott, 1957). There seems little justification for calling this condition sclerema, but in fact this was the disease for which Chaussier coined the term.

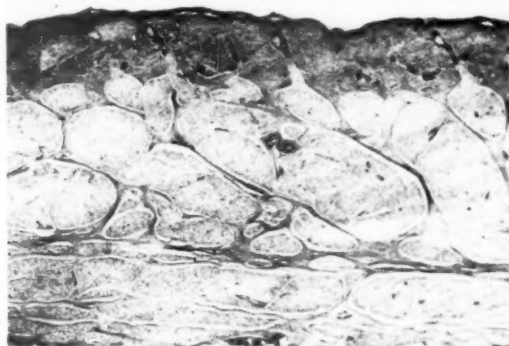


FIG. 1.—Preagonal induration: affected skin from anterior aspect of thigh ( $\times 7$ ).

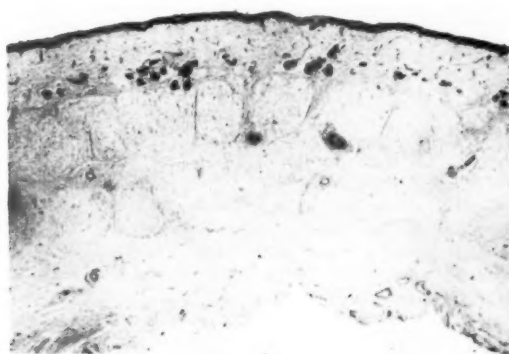


FIG. 2.—Preagonal induration: unaffected skin from upper aspect of shoulder (same case as Fig. 1). ( $\times 7$ ).

limb is not increased. When cut it has the texture of bacon rind and no fluid flows from the cut surface. The histology is less striking than in fat necrosis but none the less characteristic; the trabeculae forming the framework of the pannicular fat are broadened and the fat spaces are diminished (Fig. 1). At first sight the section suggests a fibrotic lesion but fibrosis quite evidently could not occur at the pace with which

In neonatal cold injury the striking feature is the intense erythema of the face and extremities, which belies the hypothermia, and makes a baby look the picture of health when it is in fact on the verge of death. Edema begins at the extremities and spreads centrally; although the affected skin is often hard, it almost always pits on pressure. The hardness is much less obvious after death; the tissue when cut is deeply congested and a

profuse exudate of serous fluid, tinged with blood, flows from the cut surface. Histologically the panniculus is usually thinner than in a normal child (Fig. 3); there may be congestion of dermal blood vessels but no other abnormality is found.

These then are the three interweaving strands which have been successively confused and separated at intervals over the past hundred and seventy years. The story opens with Underwood's description of "skin-bound" in 1784. The first edition of his textbook on diseases of children lacked the clarity of the classical account which appeared in the second and subsequent editions. There is no question at all, however, that what he described was preagonal induration.

In 1785 Andry in Paris described a virulent disease of the newborn which he called "Endurcissement du tissu cellulaire" (Andry, 1785). He read Underwood's first account of "skin-bound" and assumed that it was the same disease. His

come "sclerema neonatorum". This nomenclature was used by Hensch (1889) and appeared in textbooks up to the turn of the century. But then confusion was reintroduced by, of all people, Ballantyne. In 1890 he had reported two cases which demonstrated clearly the differences between oedema neonatorum (cold injury) and sclerema neonatorum ("skin-bound"). Later he noted that, "Whilst the disease has been met with and described in Great Britain, Germany, Austria, Russia, Spain, Switzerland, and the United States, it is infinitely more common in France and Italy. In fact it is an extremely rare malady in the first-named countries" (Ballantyne, 1895). Because of this lack of experience Ballantyne accepted the Italian view that there was no distinction between "oedema neonatorum" and "sclerema neonatorum". Thereafter "oedema neonatorum" disappeared from the literature and "sclerema neonatorum" remained as a label for both conditions.

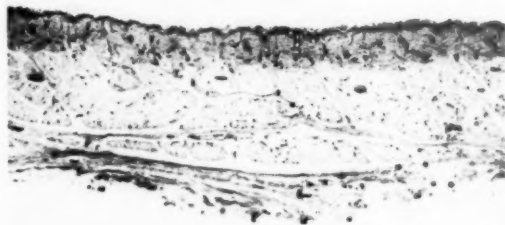


FIG. 3.—Neonatal cold injury: skin from anterior aspect of thigh. (—7.)

own paper aroused so much interest that the Société Royale de Médecine in Paris offered a prize of £600 for an enquiry into the cause and cure of the condition. This was won by Auvity who concluded "It appears evident that exposure to atmospheric cold is the sole, and sufficient cause of *endurcissement du tissu cellulaire*" (Auvity, 1788).

However, public apathy persisted and cases of "endurcissement" continued to be seen; the disease was still topical when Chaussier proposed the new title for it in 1815. "Sclérème" undoubtedly at this stage meant cold injury; but the French regarded this as synonymous with "skin-bound". Underwood himself remained convinced that the two conditions were separate, but it was not till 1877 that this view was again propounded, by Parrot in his work on "Athrepsia"; and by this time "sclerema" had undergone a change. Neonatal cold injury had become "oedema neonatorum"; "skin-bound" had be-

come "sclerema neonatorum". Meanwhile a further complication was developing. In 1845 Thirlall described a condition which he called "sclérème des adultes", which was in fact subcutaneous fat necrosis. Sporadically over the next fifty years one finds single case reports of healthy infants with localized lesions which from the descriptions were clearly subcutaneous fat necrosis; Ballantyne included many of them in his review as examples of sclerema. Fabyan, who is usually credited with the first description of subcutaneous fat necrosis was unaware of its earlier existence under another name (Fabyan, 1907). The next landmark was an address by Gray to the Golden Anniversary Meeting of the American Dermatological Association (Gray, 1926), in which he propounded very ably the view that subcutaneous fat necrosis and sclerema were the same disease. Other forms of sclerema he classified first as "acute sclerema", then later (Gray, 1933) as "preagonal induration", a term which had been used by Ballantyne.

During the previous thirty years there had been numerous reports of "sclerema" (Blacker, 1898; Bunch, 1898; Pringle, 1899; Fox, 1904; Graham-Little, 1914; Stowers, 1917), every one of them, in fact, subcutaneous fat necrosis; so that Gray was simply stating the orthodox view of English dermatology at that time and, indeed, to-day's current usage as well. The only remedy for this impasse would seem to be to drop the term "sclerema," responsible for the confusion, and use the alternative names which are available.

The normal panniculus consists of a large amount of inert material, enclosed in a delicate meshwork formed by the cell membranes of the adipose cells and supported at intervals by fibrous trabeculae. Tracer studies have shown that there is continuous interchange between depot fat and metabolic fat (Schoenheimer and Rittenberg, 1935; Hawk *et al.*, 1954). This interchange must be mediated by the adipose cell envelopes. If these are damaged, as in subcutaneous fat necrosis, the depot fat is treated as a foreign body and removed phagocytically. Considerable local inflammation occurs which, if left alone, ends in complete healing. There is no need to postulate any chemical change in the fat itself; it is not, as I see it, true fat necrosis, but adipose cell necrosis—due to trauma, local anoxemia, or some such cause—which is responsible for this condition.

In preagonal induration attention has again largely been focused on the fat; this time, I think, wrongly. A favoured hypothesis is that the hardening in this condition is due to a shift in composition of the fat from unsaturated to saturated fatty acids—a decrease in the oleic and a rise in the stearic and palmitic acids. As the infant cools, the fat then solidifies (Hughes and Hammond, 1948). The weakness of this is that complex mixtures of fats, such as human body fat, or butter, do not solidify in such an abrupt way. The melting point is spread out over a range of 10° C. or more, and there is a wide range of plasticity of texture below the melting point. In a normal infant, non-pittable hardening of the pannicular fat cannot be produced until temperatures close to freezing point are reached; and even then the texture is quite unlike preagonal induration.

The histological findings suggest an alternative explanation. The difference between affected (Fig. 1) and unaffected (Fig. 2) areas of skin in an infant with preagonal induration is the thickness of the fibrous trabeculae. The broadening they undergo cannot be the result of increased collagenization because of the speed with which it occurs; it must therefore be due to inflation of the existing tissue, a form of turgor. Really tense inflation of resistant tissue could produce the

exceptional hardness found in this condition; it is difficult to visualize any other process that would. I conclude that preagonal induration is a special form of oedema, affecting the fibrous supporting tissue of the panniculus instead of the loose intercellular spaces.

In neonatal cold injury, the hardening is much more evidently due to oedema. The tissue always pits, and when cut exudes a large amount of fluid. In spite of these typical features, it tends to be harder than most other forms of infantile oedema; but this hardness is not specific to cold injury, so that the use of a special term (e.g. scleroedema) to describe it is confusing.

The crux of the problem of cold injury, however, lies not so much in the hard oedema as in the peculiar geographical distribution observed by Ballantyne, which runs counter both to isotherms and to common sense; and in the almost inevitable corollary that only a small proportion of infants exposed to cold develop the disease. It seems that, important though it is, environmental cold is not the only aetiological factor.

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**BCG Vaccine: Nine Years' Experience at a Chest Clinic [Summary]**

By B. G. RIGDEN, M.R.C.S., L.R.C.P.

*Brighton*

BETWEEN July 1950 and the end of 1958 BCG vaccine was given to 664 persons attending the Lewes Chest Clinic, which serves a mixed urban and rural population of some 50,000 persons. Of those vaccinated 642 were under the age of 16. Follow-up to the present time has been carried out wherever possible—though 90 of the 664 have left the area at varying intervals following vaccination.

None of those vaccinated has, so far as is known, contracted tubercle.

Reversion to tuberculin anergy has occurred in 30 cases—in 8 cases only after five or more years of allergy, and in 7 cases after two years or less. Inadequate vaccination is thought to be the cause of 2 of the cases where there was only a short-term conversion period: in the other cases no explanation has been found.

The only complication encountered has been enlargement of regional lymph nodes. That occurred in 22 children, of whom only 5 required treatment. No constitutional upset was seen after vaccination.

There was a family or a close contact history of tubercle in 643 of the cases and 113 of those vaccinated came from homes where there had recently been an infectious case. 29 of the vaccinees were exposed to infection *after* immunization.

As nearly all the child contacts attending the clinic were vaccinated, there has been no adequate unvaccinated group to serve as controls. Primary tubercle has been found amongst the unvaccinated few, however, and it is considered that BCG vaccination has been a useful and simple protective measure.

**Pathology of Infantile Hypertrophic Pyloric Stenosis**

By P. A. LANE-ROBERTS, F.R.C.S.

*Brighton*

THIS enquiry was stimulated by the apparent ignorance of the cause of infantile hypertrophic pyloric stenosis. The macroscopic anatomy (Hirschsprung, 1888), the clinical course, and the management are well understood. The modern operative treatment is that of Ramstedt (1912), guided by Nicoll (1906) and Frédet and De four (1908). The results of treatment are very good.

*Material.*—From August 1955 until April 1959, 70 pyloromyotomies were performed at the Royal Alexandra Hospital without a death. In one of these cases the diagnosis was not confirmed at operation, but the vomiting was relieved, as in a case reported by Cameron (1925). In one further case the diagnosis was proven, but no operation was performed. Biopsy was done in 28 cases, and the segments of the abnormal pyloric muscles were examined.

Post-mortem material has not been available, and such museum specimens as have been examined have been too old to show cell structure.

*The normal pylorus.*—Cunningham (1906) described well the normal pyloric musculature. The longitudinal coat is uniformly dispersed around the pyloric canal. The more superficial fibres continue over the pyloroduodenal junction, but the deeper fibres leave the surface, penetrate the pyloric sphincteric ring in distinct fasciculi, and end in the bundles of the inner circular coat, or deep to them. The inner coat is a concentra-

tion of the circular muscle fibres of the stomach in the length of the pyloric canal, a concentration comparable only to the arrangement of the internal sphincter of the anus. There is no continuity between the circular muscle of the stomach and of the duodenum.

Muscular co-ordination is maintained by Auerbach's myenteric plexus of nerve fibres and ganglia, which lies between the longitudinal and circular muscles. The development of this plexus has been examined by Friesen *et al.* (1956). At the 12th week of foetal life there is a continuous layer of immature nerve cells, which by the 26th week is organized into definite ganglia. The nerve cells are still immature, but a few show vesicular nuclei. Mature nerve cells do not appear until two to four weeks after birth; these are recognized by their abundant cytoplasm, prominent cell and nuclear membranes, and distinct nucleoli.

*The abnormal pylorus.*—The biopsies were taken during Ramstedt's operation by incising the muscle parallel to the pyloromyotomy, and deepening this to meet the original incision as near the submucous layer as possible. Biopsy included the two layers of muscle and the enclosed Auerbach's plexus.

The gross hypertrophy of both muscle layers was well shown—a true hypertrophy due to overwork.

Auerbach's plexus was carefully examined and compared with normal ones from a similar age group. No special staining methods were used. Two aspects were considered, the quantity of the ganglia and the quality of the contained cells. The size and number of the ganglia varied widely in both the normal and the abnormal pylorus. In both, two to three ganglia could be seen in most low-power fields, but in the abnormal ones the size of the ganglia tended to be smaller, and the intervals between them greater. In the normal pylorus it was easy to find ganglia arranged in large continuous sheets occupying almost the entire low-power field; such ganglia were never found in the biopsy specimens. In general, therefore, the quantity of ganglion tissue was less in the abnormal pylorus than in the normal.

A ganglion contains nerve cells, supporting cells of Schwann, and nerve fibrils. In the abnormal these cells were more tightly packed. Fewer well-differentiated nerve cells were to be found. The majority of the nerve cells took more stain, and contained less cytoplasm, although normal cells were to be found in varying numbers. There was no obvious relation between the number of normal nerve cells and the age of the subject at the time of operation.

**Discussion.**—The background of any enquiry into infantile hypertrophic pyloric stenosis must be a consideration of the natural history of the disease. This is not congenital, but is acquired in the first few weeks of life. If the obstruction to the flow of food from the stomach is not so severe as to kill the infant, or if it is relieved by medical or surgical treatment (other than a bypass operation), the pylorus returns to normal. There is a genetic factor in the aetiology; 5 of these 70 cases had a family history and 1 was of the second generation.

It has been postulated for many years that the cause of the work hypertrophy of the pylorus is a neuromuscular inco-ordination (Cameron, 1925). Changes in Auerbach's plexus may account for this inco-ordination, and such changes have been reported by others.

Belding and Kernohan (1953) reported changes in the nerve cells of the plexus, which they

believed to be due to degeneration. They used autopsy material, which may not be reliable because the great killers have been gastroenteritis and the results of sepsis. Alarotu (1956) studied biopsies, and confirmed this finding. He suggested that the degeneration was due to necrobiosis as a result of overstimulation by the vagus nerves. If this were the cause, however, it is difficult to understand how the process could be reversible, and normal peristalsis resumed.

Friesen *et al.* (1956) believed the changes to be evidence of delayed maturation of the nerve cells of the plexus. If this were so, one would expect a greater incidence of hypertrophic pyloric stenosis in premature infants. No such increased incidence is reported, and there is none in this series.

**Conclusions.**—In infantile hypertrophic pyloric stenosis there are quantitative and qualitative changes in the ganglia of Auerbach's plexus of variable degree.

These changes are the reason for a phase of neuromuscular inco-ordination when the infant starts to feed. The inco-ordination results in ineffectual contractions of the pyloric muscles and a work hypertrophy. This in time blocks the pylorus in most cases.

The disturbance of function may be relieved by the natural adaptive processes of the gastrointestinal tract, in which case the tumour will soften and relax as normal peristalsis is successfully achieved. Recovery is accelerated by surgical decompression, or sometimes by pharmaceutical means.

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#### CASES

##### Recurrent Hypoglycæmia, Hamatemeses and Ketonuria in Identical Twins.—TREVOR P. MANN, M.D.

*Twin I.*—C. A., female, born 17.5.55.

Normal delivery; birth weight 5 lb. 10 oz. Three cyanotic attacks between fourth and seventh days—rigid and staring during one. Thereafter healthy until aged 17 months when she and identical twin (L. A.—see below) both started vomiting altered blood shortly after rising

one morning; both normal within twenty-four hours.

*Just before the third birthday* she (and her twin) again vomited altered blood shortly after waking; both were promptly admitted to hospital. Full recovery by following day. Barium meal normal; no cardiac enlargement. Iron deficiency anaemia. Still no precise diagnosis.

*Aged 3 years 2 months* further attack of vomiting (bile at first; then blood) at beginning of the

day. On this occasion vacant-looking and limbs stiff. Semi-comatose and very irritable on admission (two hours after onset); vomiting small amounts of altered blood. Ketouria. Normal next day without specific treatment.

(Twin had been discharged previous day following 15-day admission for similar brief episode.)

*Aged 3 years 4 months* convulsive arm movements shortly after waking in morning. Later a generalized convulsion; admitted in coma with twin in the same condition. Blood sugar less than 10 mg.%. Dramatic and immediate response to glucose. Week after recovery glucose tolerance test performed—low curve. Liver function tests normal.

*Aged 3½ years* cut her mouth on rising and refused breakfast. Shortly after inaccessible and vomited glucose water. On admission vomiting blood; conscious but hyper-irritable; blood sugar 15 mg.%; severe ketouria. Responded quickly to intravenous therapy. (Twin admitted following day with same picture. For the two months previous to this attack both had been eating well; good protein intake.) On recovery, ten days later, serial blood sugars after prolonged fasting showed lowest value 39 mg.% after seventeen hours' starvation (no ill effects from test). Repeat glucose tolerance test (twelve-hour fast; 20 grams of glucose) gave low curve; highest value 95 mg.% at two hours.

*Aged 3 years 8 months* admitted with twin for investigation. Healthy and on high-protein diet. Amino-acid-sensitivity test normal. Insulin sensitivity after fourteen-hour fast; one hour after 3 units of soluble insulin subcutaneously (0.25 unit per kg. body weight), both twins had convulsions and coma with blood sugar less than 10 mg.%.

*Aged 4 years* insulin-sensitivity test repeated after six-hour fast; again coma with twitching. Demonstrated insulin hypersensitivity.

*Aged 4 years 1 month:* Again admitted in coma. No spontaneous attacks for six months. Blood sugar less than 10 mg.%. Blood sodium, potassium and chlorides normal. Full recovery within twenty-four hours.

*At present* on high-protein, low-carbohydrate diet. Not on steroids. Serial weight values around 16-percentile. Recent height 38½ in. (also 16-percentile). Normal mentality. Between attacks no abnormal physical signs. Liver size and function tests remain normal. Serum alkaline phosphatase 22.8 units. Adrenaline-sensitivity test normal. 17-ketosteroids normal. Blood groups support uniovular twinning.

*Twin II.*—L. A., female, born 17.5.55.

Normal rapid delivery; birth weight 6 lb. Third day of life convulsive movements and frothing at

the mouth. Phenobarbitone for one week. Thereafter healthy until aged 15 months when one morning between 8.0 and 9.0 a.m. she became inaccessible and rolled her eyes. After an hour vomited brown fluid several times. Fully conscious on admission a little later. Altered blood found in gastric juice. Marked iron deficiency anaemia. Twin C. A. well at this time except for similar blood picture.

*Aged 17 months:* Further similar attack in morning. Became lifeless; eyes glazed. Vomiting followed. Twin concurrently started vomiting altered blood. Both normal within twenty-four hours.

Five admissions in 1958 for convulsive episodes commencing shortly after waking; all closely followed by repeated small haematemeses. On two occasions twin admitted at same time with identical symptoms. On three occasions profound hypoglycaemia (blood sugar less than 10 mg.%) found on arrival at hospital. Serum sodium and chloride levels normal at beginning of attack; alkali reserve 30-40 vols.% CO<sub>2</sub>. Severe acetonuria usual in first specimen tested. Quick response to intravenous glucose and full recovery within twenty-four hours.

*Investigations.*—Findings essentially similar to those in her twin (coma precipitated by first insulin sensitivity test). Liver function test normal except alkaline phosphatase 29 units (normal 3-13 units). 17-ketosteroids normal. Adrenaline-sensitivity test normal.

*Aged 4 years 3 months.* On high-protein, low-carbohydrate diet. Not on steroids. No spontaneous attacks for nine months. No abnormal physical signs between episodes. Serial weight values around 16-percentile. Recent height 39½ in. Liver size and function tests remain normal. Alkaline phosphatase 24 units. 17-ketosteroids normal. Blood groups support uniovular twinning.

#### Study of a Microcephalic Midget of Extreme

Type.—TREVOR P. MANN, M.D., and ALEX RUSSELL, O.B.E., M.D., M.R.C.P.

K. B., female, born 3.8.57.

*History.*—Ante-natal: Hyperemesis during first trimester and again in last month of pregnancy. One incident of vaginal bleeding at about three months' gestation. Fundus never rose above the umbilicus. Normal birth a few days beyond term. Considerable difficulty in removing placenta. Birth measurements: length 15.5 in.; head circumference 10.25 in. Weight 3.5 lb. Subsequent weight gain always very slow. Thus at 5 months weighed 6 lb.; at 13 months 7 lb. 11 oz.; at 16 months 8 lb.

Milestones: Sat well at 6 months; standing with

support 13 months and walking shortly after this. Always hyperkinetic.

Anterior fontanelle closed at 8 months.

*Past history.*—Prone to frequently recurring upper respiratory tract infections.

*Family history.*—Mother 5 ft. 2 in. Father 5 ft. 7 in. Maternal grandmother 5 ft. 2 in. Paternal grandfather 5 ft. Paternal great-grandmother less than 5 ft. Distant relative on each side of family less than 4 ft. 8 in.: one living, the maternal great-aunt, was 4 ft. 6 in., but with dorsal hump and no microcephaly. Clinodactyly trait, also traceable through the maternal grandfather, is represented in the family independently of growth deficiency.

Second baby born September, 1959—a normal female infant.

*On examination.*—Alert hyperkinetic microcephalic midget. Rodent- or ferret-like profile with the microcephaly, her receding chin and small mouth surmounted by a prominent nose (Fig. 1.) Incurved little fingers with underlying hypoplasia of the middle phalanx. Some retinal pigmentation.

*Mental developmental status:* 15–18 month level (chronological age: 25 months).

*Growth status:*

*Height* now 5.25 in. below 3-percentile and 3.75 in.  $< -2\sigma$

(At 15 months 7.0 in. below 3-percentile and 6.5 in.  $< -2\sigma$ )

*Bone age:* At 8 months equivalent to birth level.

At 15 months } i.e. slightly in  
= 3 months } advance of  
At 2 years = } the height age  
6–9 months }

*Hypothalamo/pituitary/adrenocortical function.*  
—The lowness of basal levels of urinary ketogenic steroid output of 0.5–1.0 mg./twenty-four hours but sharp rise on ACTH stimulation, viz. already thirteenfold increase by the third day, suggested an endogenous deficit of an adrenotrophic factor.

This may also have been reflected in the exceptionally flat five-hour glucose tolerance curves after a glucose load of 1.75 g./kg. body weight, with hypoglycaemic trends from the third hour provoked by increasing the glucose load to 2.5 g./kg.

TABLE I.—FIVE-HOUR GLUCOSE TOLERANCE CURVES  
(Blood sugars in mg. % (true))

	First	30 min.	60 min.	90 min.	120 min.	3 hr.	4 hr.	5 hr.
Glucose load: 1.75 g./kg.	65	74	71	67	68	67	59	65
Glucose load: 2.5 g./kg.	73	78	92	85	83	55	54	51

There was also an unusual rise in serum sodium concentrations during the ACTH test, although without significant modification of serum or urinary sodium/potassium ratios: thus levels rose from the relatively low 131 mEq./l. to 140 mEq./l. on the third day and 143 mEq./l. by the fifth day of stimulation. One can only speculate as to whether an endogenous deficit of more than one hypothalamo-pituitary factor may be involved.

*Hypothalamo/pituitary/thyrotrophic activity.*—The indices of thyroid function (Table II) indicated high basal endogenous T.S.H. stimulatory activity, although the  $^{131}\text{I}$  neck uptake fell short of thyrotoxic levels; there was no goitre and the eyes, albeit prominent and characteristically staring

GROWTH DIMENSIONAL RELATIONSHIPS

	Actual dimensions at 2 years	Relationships to:			
		Age standards		Length standards	
		At 15 months	At 2 years	At 15 months	At 2 years
Length	26.25 in.	7 in. $< 3$ -percentile = 1 month height age	5.25 in. $< 3$ -percentile = 6 months height age		
Span	26.25 in.	7.7 in.	5.8 in.	+0.5 in.	+1.25 in.
Lower segment	11.5 in.	1.85 in.	2.6 in.	+2.25 in.	+1.25 in.
Circumferences:					
Head	13.25 in.	6.25 in.	5.75 in.	2.7 in.	4.15 in.
Thorax	14.0 in.	5.4 in.	5.2 in.	1.1 in.	3.1 in.
Abdomen	14.0 in.	5.4 in.	4.6 in.	1.1 in.	2.9 in.
Weight	9.7 lb.	1.5 lb.	1.5 lb.	1.6 lb.	6.5 lb.

#### Investigation

A full-scale endocrine-metabolic study was completed at The Queen Elizabeth Hospital for Children, London, despite the peculiarly agitated and mercurial character of the subject. Deviations from the normal of significant degree were as follows:

fixedly in quizzical fashion, were not exophthalmic.

Thus basal two- to six-hour neck uptake of  $^{131}\text{I}$  approached the upper limit of normal, whilst the modification by five days of T.S.H. stimulation was relatively poor at four hours and negative at six hours (Table II).

TABLE II.—FIVE-DAY T.S.H. TEST

	Pre-T.S.H.			Post-T.S.H.		
Serum cholesterol (mg./100 ml.)	124			121		
Serum P.B.I. ( $\mu$ g./100 ml.)	7.4			7.9		
	2 hr.	4 hr.	6 hr.	2 hr.	4 hr.	6 hr.
<sup>131</sup> I % Neck uptake	10	25	44	21	35	35

Unexpectedly high serum alkaline phosphatase activity in the presence of such extreme growth failure (range 21.7 to 24.9 K.-A. units) may be another expression of high thyroid activity; no other explanation was found.



FIG. 1.—K. B. To show beaked nose and small head (circumference 13½ in.).

#### Comment

**Investigation results.**—A fundamental disharmony of cerebral/diencephalic regulation is indicated in the paradoxical association of hyperkinesia and apparently high basal metabolic and thyrotrophic activity with extreme deficiency of growth and evidence implying an endogenous deficit of one or more adrenotrophic factors. Clarification of the basis of this pattern must await precise definition of the nature of the cerebral dysgenesis associated with gross microcephaly.

**Growth-failure category.**—In her birth-weight of 3.5 lb. and length of 15.5 in. despite even post-mature gestation, and in her uniform leanness and bilateral clinodactyly our case recalls the "intra-uterine" dwarf series (Russell, 1954). Each also has a prominently developed nose, especially the nasal bridge, evident from birth, and hyperactivity, although both aspects are more extreme

in our case. Elongation of lower extremities relative to the trunk is seen in both types, although in the intra-uterine series there is contrasting relative shortening of the upper limbs.

But the craniofacial proportions immediately single out this type of case: smallness of the cranium is at once conspicuous (head circumference at birth 10.25 in.), whereas the Russell type is typified by an illusion of hydrocephalus with the head size at birth proportionate in size or even slightly in excess of that appropriate to the body length. By contrast, the head circumference in our case still did not exceed 12.25 in. at 15 months or 13.25 in. after 2 years, both dimensions almost 6.0 in. below that appropriate to the length, or achieved in the intra-uterine series at corresponding ages. Another distinctive cranial feature is her early anterior fontanelle and suture closure (viz. at 8 months), the intra-uterine group being marked by delay in closure extending into the third year of life. *Respective*



FIG. 2.—Caroline Crachami (Home, 1828). A microcephalic midget. From a painting in the Museum of the Royal College of Surgeons. Both craniofacial and skeletal proportions corresponded closely with those of the case described.

*progress in growth* also separates them even within their first year for whilst K. B. was actually 1.0 in. longer at birth than two of Russell's series, by 15 months the latter had typically reached 25 to 26 in., and by 2 years about 30 in., whereas K. B.'s corresponding attainments were 21.5 in. and 26.25 in.

In other categories of lean dwarfing with microcephaly both components are much less extreme (excluding gross microcephalic amentia): for example, in primordial microcephalic dwarfing of strongly familial incidence (Upjohn, 1955); in the Fanconi type (1927) with its associated digital and other anomalies and eventual skin hyperpigmentation, with or without significant haematopoietic disorder, and in the progeroid dwarfing of Cockayne-Neill type (Neill and Dingwall, 1950), distinguished in addition by stigmata of pseudo-senilism, intracranial calcification, and

both relative elongation (distalward) and increased covering of upper and lower extremities.

Examples of comparably extreme growth depression and microcephaly are indeed very rare, but adequately documented records of sporadic cases are traceable well back into the nineteenth century. Caroline Crachami's skeleton and portrait—the microcephaly and large nasal protuberance in profile so closely resembling K. B.—are still to be found in the Royal College of Surgeons (Fig. 2). A more adequately documented prototype was presented by Magitot in 1881: Ed. Placereau born in 1867 being so small at birth "that he could be enveloped in a pocket handkerchief". At 14 years of age, his height was only 93 cm. (36.5 in.) and his head circumference 15.75 in. The extraordinary length and volume of his nose was noted. Agitation, distractibility and hyperkinesia have characterized them all.

#### *Ætiology, &c.*

Genetically our case could have been a product of abnormal recessive growth genes issuing from both sides of the pedigree, with microcephaly—not apparently hitherto represented—possibly a superadded sequel of this encounter. The clinodactyly is another possibly dissociated trait since its heredo-familial incidence independently of growth-failure was traced back to the maternal grandmother and beyond.

A possible basis of chromosomal aberration may yet be defined, although in view of the bleeding incident in the third month of gestation, embryopathic considerations are not entirely overruled.

To what extent the relative decline in post-natal growth progress is related to the gross microcephaly and/or to an underlying cerebral dysgenesis remains to be resolved. Nor is it known if any primary premature craniosynostosis is involved, and as a corollary whether linear craniectomies could contribute relief to the post-natal depression of both growth and cerebral development.

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#### **Congenital Bowing Left Tibia and Fibula.—**

AUSTIN BROWN, F.R.C.S.

S. S., female, born 15.2.57.

Full-term, normal delivery. The left foot was lying on the lateral aspect of the lower leg in a concavity formed by a marked bowing of the tibia, open antero-laterally (Fig. 1).

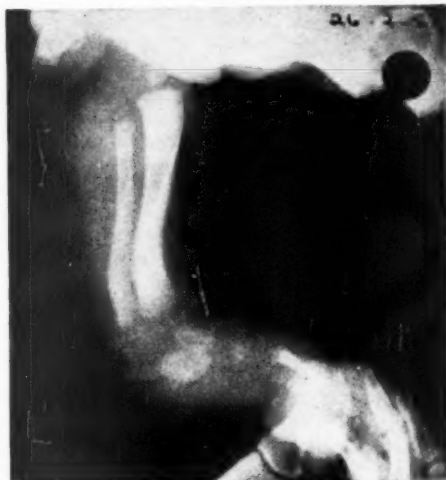


FIG. 1

The appearances are similar to a congenital pseudarthrosis although the angulation in this condition is usually open posteriorly.

Apart from a light plaster slab which was worn for ten weeks the child has had no treatment. The deformity is decreasing in severity and will continue to do so. The only residual deformity one would expect is a little shortening of the lower leg (Heyman *et al.*, 1959).

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#### **Atresia of the Pyloric Antrum.—**L. W. LAUSTE, F.R.C.S., and W. MESTITZ, M.D.

M. M., male, born 1.7.58.

*History.*—Admitted aged 4 days. Full-term normal delivery. Birth-weight 6½ lb. Second baby. Mother Rh-positive; had hydramnios during last two months of pregnancy. Vomited since first put to breast, either during feed, or within twenty minutes. Vomiting not projectile but seemed to be the whole feed. No bile in the vomit. Passed very little meconium and this was slightly blood-stained. Urine scanty. Losing weight.

*On examination.*—Vigorous baby, slightly jaundiced. High-pitched cry. Fontanelle depressed; tongue dry. Heart and lungs normal. Abdomen not distended; no peristalsis visible and no tumour felt. Rectal examination normal.

*Investigations.*—Plain films of the abdomen in the erect and supine positions showed complete absence of any gas shadow except in the fundus of the stomach; the stomach appeared to contain fluid.

*Treatment.*—Operation under local anaesthesia on fifth day revealed that the stomach was dilated, the pyloric antrum replaced by a tubular cord of tissue and the pylorus was thought to be felt distally. The duodenum was normal, the gall-bladder distended, the transverse colon showed a fusiform dilatation in the middle and the remaining colon and all the small bowel were collapsed. The stomach was opened anteriorly and found to end blindly. A posterior gastro-enterostomy was performed.

*Progress.*—This was slow; the obstruction persisted for seven days but was suddenly overcome. Thereafter the baby made a rapid recovery.

Atresia of the stomach appears to be extremely rare and only four cases have been found in the literature (see references).

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- The following cases were also shown:
- (1) **Vascular Ring.** (2) **Congenital Syphilis.**—Dr. TREVOR P. MANN and Mr. P. V. WADSWORTH.
- Sacroccygeal Teratoma in a Newborn.**—Mr. L. W. LAUSTE and Dr. W. MESTITZ.
- (1) **Tricuspid Atresia.** (2) **Persistent Oedema of Feet: Cause Unknown.** (3) **Tuberculous Pericarditis.** (4) **Infective Polyneuritis (Guillain-Barré Syndrome).**—Dr. W. MESTITZ.
- (1) **Achondroplasia Buphthalmos.** (2) **Angioma of Ciliary Body with Skin Angiomata.**—Mr. M. J. GILKES.
- Familial Acholuric Jaundice—Congenital Hypertrophic Pyloric Stenosis.**—Dr. W. MESTITZ and Mr. P. A. LANE-ROBERTS.
- (1) **Chicken-pox Encephalitis with Hypoglycaemia.** (2) **Rubella Syndrome.** (3) **Lumbosacral Meningomyelocele.** (4) **Moderate Hydrocephaly.** (5) **Arnold-Chiari Malformation.** (6) **Skull and Scalp Defects.** (7) **Lymphosarcoma of Mediastinum.** (8) **Aplastic Anaemia.** (9) **Epilepsy.** (10) **Self-induced Minor Attacks.** (11) **Marfan's Syndrome.**—Dr. TREVOR P. MANN.
- (1) **Fibrocystic Disease of Pancreas.** (2) **Jejunal Atresia.** (3) **Two Cases of Bizarre Developmental Syndrome which includes Symptomatic Hypoplasia of one Thenar Eminence, Absence of the Related Radial Pulse, Undescended Testicle and Renal Abnormalities.**—Dr. TREVOR P. MANN and Mr. P. A. LANE-ROBERTS.
- (1) **Megacystis-mega-ureter.** (2) **Bilateral Ectopic Ureters.** (3 and 4) **Two Cases of Giggle Incontinence.**—Mr. S. H. C. CLARKE.
- (1) **Monostotic Fibrous Dysplasia.** (2) **Massive Calcification with Left Sesamoid-metatarsal Bursa.** (3) **Valgus Deformity Left Foot.** (4) **Extra-articular Talo-calcaneal Fusion.** (5) **Healed Perthe's Disease.** (6) **Calve's Disease.** (7) **Mother with Osteochondritis Dissecans.** (8) **Her son with Perthe's Disease Right Hip.** (9) **Chronic Osteitis Left Femur Simulating Neoplasm.**—Mr. AUSTIN BROWN.
- (1) **Traumatic Right Hemiplegia.** (2) **Intracerebral Hematoma.** (3) **Cerebellar Glioma.**—Mr. F. L. DAVIES.
- (1) **Left Tympanoplasty for Deafness.** (2) **Mild Right Hemiplegia.** (3) **Left Tympanoplasty.**—Mr. P. V. WADSWORTH.
- Two Cases of "The Catlin Mark" (Fenestra Parietales Symmetrica).**—Dr. TREVOR P. MANN and Dr. J. RUBIN.
- The "Ovingdean skull" (on loan for the Brighton Museum through the kindness of Mr. Clifford Musgrave) was exhibited alongside these two cases. The skull defects which this specimen shows are alleged to be due to primitive trepanning.
- Carcinoma of Thyroid Hypoparathyroidism.**—Mr. P. A. LANE-ROBERTS and Dr. C. BARRINGTON PROWSE.
- Dermatomyositis.**—Dr. COLIN JONES.

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Chairman—JOHN T. INGRAM, M.D., F.R.C.P.  
(President of the Section of Dermatology)

Meeting  
May 7, 1959

JOINT MEETING AT THE HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON

**Acrodermatitis Enteropathica.**—J. B. LYON, M.D.,  
M.R.C.P.

B. W., male, aged 10 years.

**History.**—At 6 weeks of age, vesicular eruption on face, forehead, neck and buttocks, occurring in crops every few days, up to the age of 3 years, then replaced by desquamating psoriasiform lesions with fissuring around the orifices, nail deformity and complete alopecia. Intermittent diarrhoea; irritable, ill and photophobic, with secondary skin infection.

**Clinical findings.**—When aged 5 years, under-weight, miserable, photophobic, complete alopecia, extensive red desquamating lesions, including hands and feet, with deformed nails. Fissuring corners of mouth, ulceration buccal cavity. Teeth normal. Other systems showed no abnormality.

**Investigations.**—Monilia in stools and mouth, no pathogenic bacteria. Skin lesions showed *Staph. pyogenes* and monilia.

**Treatment and progress.**—Diodoquin 210 mg. daily, increased to 600 mg. q.i.d. Skin, hair and nails improved after a few weeks but after two months sterile bullæ and scaly dermatitis returned but without diarrhoea. Health gradually improved after long hospitalization.

Remains well, though under-weight, on Diodoquin 300 mg. q.i.d. Hair growth normal, teeth rather carious, nails still somewhat dystrophic. Scaly patch left ankle, some milia on neck. Slightly backward at school.

**Comment.**—Reduction of Diodoquin to 300 mg. b.d. resulted in a relapse within one week, with scaling and crusting of the upper lip, neck and left ankle, but without pathogenic bacteria or monilia.

This boy was previously shown by Dr. I. S. Hodgson-Jones (1955). At the peak of his illness, he exhibited all the characteristics of the disorder—early impetigo-like and later psoriasiform lesions around the orifices and on extremities, alopecia, nail dystrophy, recurrent diarrhoea and bouts of secondary infection by both

bacteria and yeasts. Acrodermatitis enteropathica was originally described by Danbolt and Closs (1943), their cases ending fatally. In a further series (Danbolt, 1948, 1956) the post-mortem showed minute non-specific inflammatory ulcers in the large gut. Dillaha *et al.* (1953) reported the curative value of Diodoquin which has proved life-saving in a number of patients, some being able to discontinue the drug after two months. In others a maintenance dose is necessary. Fortunately the drug appears to be non-toxic on prolonged dosage, and yet by some peculiar pharmacodynamic action, enables the gut to function normally.

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**Dr. M. Feiwel:** Dr. Schlesinger saw resemblances to fibrocystic disease of the pancreas when a case was shown to the Section of Dermatology (Hare and Schlesinger, 1956, *Proc. R. Soc. Med.*, **49**, 231).

**Two Cases of Toxic Epidermal Necrolysis.**—W. FRAIN-BELL, M.D., and P. KOBLENZER, M.R.C.P.Ed.

I.—J. G., female, aged 3.

**History.**—Admitted on 8.4.59 having been perfectly fit except for an attack of measles two months previously. Two days prior to admission swelling and redness appeared in the skin around the eyes, lips and ears, spreading the same day to involve the chest and back. On admission the skin of the body, trunk, face and limbs was extensively involved in a red "scald-like reaction" with loosening of the skin and the formation of flaccid bullæ. By 10.4.59 the loose skin had peeled off, exposing a raw red surface which was extremely tender. On 13.4.59 there was a dramatic improvement, no fresh lesions having

developed in the previous twenty-four hours. During the next few days a complete post-scarlatiniform type of exfoliation of the skin took place with the formation of the occasional small blister. She had an intermittent fever to a maximum of 104° F. from 8.4.59 until 13.4.59. Since 24.4.59 her skin has been normal and she has been fit and well.

**Investigations.**—Blood count (8.4.59): Hb 81% (11.8 grams per 100 ml.); W.B.C. 10,400 (neutros. 78%, lymphos. 18%, monos. 4%) E.S.R. 21 mm. in one hour (Westergren).

**Swabs:** Throat, 8.4.59: "A few colonies of hemolytic streptococci and a moderate growth of *Streptococcus viridans* and coagulase-positive staphylococci." (21.4.59): "Heavy growth of *Streptococcus viridans* and coagulase-positive staphylococci."

**Blister fluid from intact blister:** "No abnormal cells seen." Culture: a few colonies of micrococci.

**Skin, 8.4.59:** Gram: occasional Gram-positive cocci. Culture: a heavy growth of coagulase-negative staphylococci.

**Eye, 8.4.59:** Gram: debris only. Culture: a heavy growth of *Str. pneumoniae*.

**Nose, 16.4.59:** Heavy growth of coagulase-positive staphylococci.

**Swab from septic spot:** Gram: debris only. Culture: heavy growth of coagulase-positive staphylococci.

**Serum proteins:** 6.1 grams per 100 ml. Electrophoresis: normal pattern.

**Electrolytes (12.4.59):** Plasma bicarbonate 24, chloride 105, sodium 134, potassium 4.1 mEq./l. Blood urea 26, calcium 10.1 mg./100 ml.

**Antistreptolysin titre:** 10.4.59: 500 units/ml. 5.5.59: 333 units/ml.

**Treatment.**—Prednisolone 40 mg. daily was given from 8.4.59 to 14.4.59 when it was gradually reduced and finally stopped on 20.4.59, a total of 330 mg. having been administered. Tetracycline 150 mg. six-hourly was given at the same time.

II.—J. B., female, aged 2.

**History.**—Admitted on 23.12.58, having had two weeks previously an upper respiratory tract infection with conjunctivitis and a generalized macular rash. This was treated with a cough mixture and oral penicillin for five days, nothing being administered after 14.12.58. On 21.12.58 she developed redness of the skin of the neck and by 23.12.58 the whole body skin was extensively involved with erythema, widespread loosening and the formation of flaccid bullae which developed large raw red areas. The skin changes were identical to those resulting from "scalding". By the end of the first week she was very much

improved although a few small bullae continued to appear during the next week. A terminal universal post-scarlatiniform type exfoliation occurred. Five days before admission she had been scratched on her right cheek by a cat, the lesion being treated with Neobacrin ointment. Since her discharge from hospital on 21.1.59 she has remained well with a normal skin.

**Investigations.**—Skin swab, 23.12.58: Gram: debris only. Culture: no growth. 31.12.58: Gram: debris only. Culture: heavy growth of coagulase-positive staphylococci and diphtheroids.

Examination of urine on two occasions showed no abnormalities; cultures sterile.

**Blood count:** Hb 78% (11.4 grams per 100 ml.), W.B.C. 23,600 (neutros. 62%, eosinos. 1%, lymphos. 34%, monos. 3%).

**Treatment.**—Prednisolone was given from 25.12.58 until 1.1.59 with an initial dose of 20 mg. daily for three days, and a total dose of 100 mg.; Triamcinolone 4 mg. daily until 5.1.59; Achromycin 75 mg. six-hourly, from 24.12.58 to 31.12.58; Midicel 0.25 grams daily, from 1.1.59 to 5.1.59; and Chloromycetin 250 mg. six-hourly, from 7.1.59 to 11.1.59.

**Comment.**—Since toxic epidermal necrolysis was first described by Lyell (1956) and Lang and Walker (1956) there have been a number of additional reports in adults (Lang and Walker, 1957; Rook, 1958). It is fatal in approximately 30% of published cases although apparently it may equally well have a mild course with recurrent attacks (Rook, 1958). The aetiology is still obscure, although there is the possibility of its being a reaction to infection or previously administered drugs since Case II had had a course of penicillin and Case I a streptococcal tonsillitis. The administration of high dosages of corticosteroids in the early stages might well reduce the severity of the reaction.

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**The President:** Dr. Martin Beare in Belfast had a child who showed this reaction, who three weeks previously had had a sore throat and penicillin therapy. He received steroids and recovered. A baby, with the same condition, died; the histology showed no inflammatory reaction and I wondered if this was a generalized reaction to a virus infection similar to Ritter's disease with pyococci.

**Dr. W. Frain-Bell:** Virological investigation of the blister fluid produced negative results.

**Dr. H. Haber:** I have seen one case which clinically

presented the picture of toxic epidermal necrolysis, yet histologically showed characteristic features of pemphigus foliaceus.

The following cases were also shown:

**Scleroderma en Coup de Sabre with Cerebral Calcification.**—Dr. S. D. V. WELLER.

(1) Hebra's Prurigo. (2) Epidermolysis Bullosa (Dowling Type). (3) Two Cases of Tinea Capitis Treated with Griseofulvin.—Dr. R. H. MEARA.

(1) ? Von Recklinghausen's Disease. ? Tuberous Sclerosis. (2) Two Cases of Phenylketonuria with Eczema.—Dr. BRIAN H. KIRMAN.

(1) Pityriasis Rubra Pilaris. (2) Honeycomb Nevus. (3) Ectodermal Defect.—Dr. R. R. M. HARMAN (for Dr. R. T. BRAIN).

(1) Juvenile Dermatitis Herpetiformis. (2) Pityriasis Lichenoides Chronica for Three Years in a Child Aged 6.—Dr. JOHN EVERALL (for Dr. R. T. BRAIN).

**Hansen's Infection—Indeterminate Type.**—Dr. JOHN EVERALL (for Dr. R. LIGHTWOOD and Dr. R. G. COCHRANE).

(1) Ehlers-Danlos Syndrome: Defective Skull Ossification and Skin Collagen Formation. (2) Adenoma Sebaceum.—Dr. M. K. STRELLING (for Dr. R. T. BRAIN).

(1) Linear Epidermal Nevus. (2) Lichen Sclerosus. (3) Epidermolysis Bullosa. (4) Lichen Sclerosus.—Dr. R. T. BRAIN.

**Angioma.**—Dr. P. KOBLENZER.

**Two Cases of Eczema in Identical Twins.**—Dr. W. FRAIN-BELL and Dr. P. KOBLENZER.

**Discoid Lupus Erythematosus.**—Dr. C. J. STEVENSON (for Dr. BRIAN F. RUSSELL).

**Two Cases of Urticaria Pigmentosa in Identical Twins.**—Dr. C. J. STEVENSON (for Dr. R. T. BRAIN).

**Porokeratosis Mibelli.**—Dr. A. P. NORMAN.

**Ectodermal Defect.**—Dr. H. J. WESTON (for Dr. G. H. NEWNS).

**Macular Erythema and Chondritis.**—Professor E. G. L. BYWATERS.

**Dermatomyositis.**—Dr. B. M. ANSELL.

Dr. MARTIN BODIAN showed a series of slides illustrating the **Histiocytic Reticulo-endothelioses** from the Pathological Museum, demonstrating the fundamental inter-relationship of Letterer-Siwe disease, Hand-Schüller-Christian syndrome and eosinophilic granuloma of bone.

## Section of Dermatology

President—JOHN T. INGRAM, M.D., F.R.C.P.

### Meeting

May 21, 1959

**Amblyopia in Lupus Erythematosus.**—G. C. WELLS, F.R.C.P.

J. B., female, aged 26.

**History.**—Chronic discoid lupus erythematosus has been present for about six years. She was treated in New Zealand, and received chloroquine (200 mg. daily) and mepacrine (100 mg. daily) for at least two years, and cortisone for eighteen months. She also had injections of bismuth and gold. In 1958 she was admitted for three months for pyoderma and weight loss, and was found to have a slight leukopenia, but no definite signs of systemic disease. Difficulty with vision started about a year ago with night-blindness, and upon arrival in this country (September 1958) she could hardly walk unaided.

**Clinical findings.**—There is lupus erythematosus on the lips, buccal mucosa, face, neck, arms and backs of fingers. She can scarcely see to walk and can read only a few words at a time. Mr. Harold Ridley reported on the eyes: "In both fundi the retinal arteries are narrowed, there is some peppery pigmentation which is probably

outside normal limits, and there has been for a considerable period perimacular oedema. Acuity of the right eye is 6/18 partly and the left 6/9, but the central fields are extremely restricted though there is still some peripheral field temporally and below."

There is no abnormality of the cornea.

**Investigations.**—(1959) Hb 103%, W.B.C. 3,600 (polys. 61%, monos. 16%, lymphos. 23%). E.S.R. 8 mm. in one hour (Wintrobe). No L.E. cells have been found on repeated search. Serum albumin 4.8, globulin 1.4; decreased alpha-globulin on electrophoresis.

**Comment.**—We do not know if the severe deterioration of vision is related to the lupus erythematosus or to its treatment. The degenerative changes in the retina with narrowing of the retinal vessels (rather resembling retinitis pigmentosa) have not been described in chronic discoid lupus erythematosus, and may result from the cumulative toxic effects of antimalarial drugs such as chloroquine.

**The President:** I cannot recall any patients having lupus erythematosus with central nervous lesions. It is mostly systemic lupus erythematosus patients who have been subject to transient blindness and other neurological manifestations.

**Dr. W. G. Tillman:** I have not seen a case where neurological lesions could be attributed to lupus erythematosus, though I have seen such lesions caused by chloroquine. There was a girl who developed a weakness in the leg, but the neurologist was never able to decide whether it was neuritis or a myopathy and she recovered very rapidly when chloroquine was discontinued.

**Dr. Peter Miescher:** To my surprise, the incidence of psychoneurological complications was rather high in the group of the New York, Bellevue Hospital, patients. Many patients came first to the Psychiatric Department because of organic psychosis. In addition, some patients had periods with convulsions or with chorea.

**Dr. J. S. Pegum:** I have seen one patient who had monoplegia with disseminated lupus erythematosus and another who had retinitis of the kind described in lupus erythematosus with white deposits (cytoid bodies) on the retina. That, of course, was a frank disseminated lupus erythematosus with fatal outcome.

**Dr. M. Feibel:** Neuropsychiatric complications may occur without other systemic features. A patient with discoid lupus erythematosus developed paresis of the ocular muscles attributed at first to cerebral tumour. A psychiatric colleague, who looked out specially for lupus erythematosus in his patients, told me only yesterday that he had not found a single case. However, one hour later, a consultation card took me to see one of his mentally disturbed patients. She had discoid lupus erythematosus.

**Dr. S. G. Gold:** I can recall a patient who, during an acute exacerbation of systemic lupus erythematosus, became maniacal. We were concerned whether this was part of the disease or due to the corticosteroids she was being given. It proved to be the disease for a subsequent relapse was shown to be associated with marked changes of the electroencephalogram and these changes reverted to normal after control of the acute episode with further steroid therapy.

**Dr. H. R. Vickers:** I think this variety of extensive discoid lupus erythematosus is extremely important. One always feels that the patients are going over into disseminated lupus erythematosus in spite of what has been said. With this particular woman one wonders what are the contraindications to steroids. We have had two patients with resistant systemic discoid lupus erythematosus and they responded dramatically to small doses by mouth.

#### Weber-Christian Disease. ? A Collagen Disease.

—M. A. VEITCH, M.B. (for C. W. BARTLEY, D.M., M.R.C.P.).

M. J., aged 41. Jamaican, housewife.

**History.**—1954: Arrived in England. 1956: Appearance of painless subcutaneous lumps (chiefly breast). Admitted Lambeth Group for biopsy (*vide infra*). Lumps recurred inter-

mittently all over the body including scalp, with temporary patchy alopecia. 1957: Biopsy elsewhere (*vide infra*). August 1958 to March 1959: Treated with steroids at a third hospital. December 1958: E.S.R. 86 mm. in one hour (Westergren), serum albumin 3.1, globulin 3.89 g.%. Since November 1958 lumps painful and malaise during menses plus coughing since February 1959. Since April 1959, after stopping steroids on own initiative, persistent malaise, vomiting, fever and dull chest pain.

**On examination.**—Obese, cheerful, anæmic, diurnal fever plus rigors (104° F.) worse during menstruation, with vomiting. Subcutaneous, firm pitted nodules attached to skin, becoming swollen, hot, red and tender during menstruation. Patchy alopecia plus new hair growth. Scattered crepitations of lungs.

**Investigations.**—Urine: albumin +, with granular casts, R.B.C., W.B.C.; no Bence-Jones protein. Hb 67% (M.C.H.C. 30%). Leucocytes 3,400 (polys. 51%, lymphos. 46%, eosinos. 1%). No L.E. cells. E.S.R. 128 mm. in one hour (Westergren). Chest X-ray: Small area of mottling in both upper zones which cleared after a week. X-rays of skull, pelvis and femora normal, apart from slight hyperostosis frontalis interna. W.R., Widal agglutinations and blood cultures negative; Rose-Waaler test negative; serum albumin 2.4, globulin 4.38 grams% (excess gamma-globulin), thymol turbidity 4+, zinc sulphate 15.

**Biopsy** (1956): Decreased fat tissue, infiltration in the fat and fibromuscular layer under the dermis with many plasma cells, groups of fibroblasts and lymphocytes. Biopsy 1957 (loaned by Professor H. A. Magnus): similar changes.

**Comment.**—The interesting feature of this patient with apparent Weber-Christian disease is the presence of a generalized disorder which improves with rest and steroids. A number of cases of visceral panniculitis have been described with systemic disturbances (Oram and Cochrane, 1958). Investigations, apart from biopsy, have rarely been performed and thus systemic disturbances in other cases may have been missed. It is possible that this is a collagen disease and that steroid therapy may be of value. In this particular case, the history, physical signs and investigations strongly support a diagnosis of Weber-Christian disease with systemic manifestations, although, in the absence of fat necrosis, the histology does not confirm this.

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**Dr. Henry Haber:** The histology shows a marked round cell infiltration permeating the interstices of fat tissue. The fat cells, however, are intact, and nowhere is there any evidence of fat necrosis. The histology does not support a clinical diagnosis of Weber-Christian disease. One should perhaps consider lupus erythematosus profundus.

The following cases were also shown:

**Lupus Erythematosus in Grafted Burn Scar.**—

Dr. E. N. M. JOHNSTON.

**Chronic Discoid Lupus Erythematosus.**—Dr. M. FEIWEL.

**Lupus Erythematosus.**—Dr. W. TILLMAN.

**? Lupus Erythematosus.**—Dr. BENTLEY PHILLIPS.

**Lymphocytoma Cutis of the Right Forehead,** in a woman aged 49, of two years' duration.

Histology consistent with this diagnosis.—  
Dr. J. D. EVERALL (for Dr. G. B. MITCHELL-  
HEGGS).

**Myxœdema Papulosum.**—Dr. M. A. SMITH (for  
Dr. BERNARD GREEN).

**Hansen's Disease.**—Dr. E. N. M. JOHNSTON (for  
Dr. G. C. WELLS).

**Lichen Sclerosus.**—Dr. E. WILSON JONES (for Dr.  
H. J. WALLACE).

A Symposium was held on **Chronic Discoid Lupus Erythematosus.** The opening papers were: **Advances in the Understanding of Lupus Erythematosus.**—Dr. STEPHEN GOLD; **Immunological Aspects of Lupus Erythematosus.**—Dr. PETER MIESCHER.

#### Meeting

June 18, 1959

#### MEETING AT THE LONDON HOSPITAL, WHITECHAPEL, LONDON

**Two Cases of Hæmangioma Showing Delayed Natural Resolution.**—BRIAN RUSSELL, M.D.,  
F.R.C.P.

I.—M. R., female, aged 7 years.

**History.**—Capillary cavernous hæmangioma involving skin and mucosal surface of upper lip first noticed aged 10 days. Its progress has been followed for the past seven years.

**Clinical findings.**—Fleshy almost bloodless remnant 1.7 × 2 cm. on the upper lip.

II.—S. B., female, aged 6½ years.

**History.**—Strawberry hæmangioma first noticed at 3 weeks, on vermilion surface of upper lip, followed by fleshy hæmangioma beneath left nostril. Both became ulcerated. Began to shrink at 13 months. At 5 years a fleshy swelling remained that has not yet disappeared.

**Comment.**—In each patient the hæmangioma has disappeared, leaving a fleshy excess of tissue. I anticipate that this too will disappear in time. I have not myself seen hæmangiomata which have eroded bone and I would like to hear the experience of others.

**Dr. R. H. Seville:** I have followed up similar cases for five years and have been satisfied with the result of leaving them alone; none has ended in surgery.

**Dr. F. F. Hellier:** I feel unhappy about these cases. The hæmangiomata probably disappear in time, but for a child to have a severe blemish on its face, or in some other visible part, up to the age of 5 or 7 is a terrible handicap. We know what children are. When they see another with a blemish, they say, "Don't go near that little girl, she has a mark on her face". Psychiatrists tell us that such things happening in childhood may have serious effects in later life. I have seen little children with such blemishes walking

about trying to hide the affected part of the face. We have no right to let children with exposed birthmarks go through seven years of life suffering what is really psychological trauma. Any conspicuous lesion should be treated. I treat strawberry marks and other such marks on exposed areas because I feel it is fair to both child and mother.

**Dr. N. A. Thorne:** What does Dr. Brain consider to be the maximum dosage of X-rays that can safely be given in treating such cases? When these lesions occur over growing epiphyses is there danger of shortening of a limb if X-ray or radium therapy is given in early life? I have always subscribed to the view that we should leave these lesions alone.

**Dr. R. T. Brain:** I support Dr. Hellier. My practice when these marks are obvious is to give X-rays, in doses of 250–300 r, at monthly intervals, practically never exceeding the total of 1,000 r. One sees no atrophy as a result of that treatment, although atrophy occurs in the case of large lesions whether treated or not. There is redundant, pale, wrinkled skin which needs trimming up, and that is a matter of simple excision. In a reported series of 614 cases (Brain and Calnan, 1952) 147 lesions were untreated and they cleared up nearly as well, although not so quickly. I would treat the blemishes if exposed, but not if they are out of sight or on the scalp.

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**The President:** Does Dr. Brain feel that these particular cases if treated with radium therapy early in life would escape the deformities that appear later?

**Dr. R. T. Brain:** I would not think it fair to say that. When the lesions are large there is often redundant flabby skin, which has to be trimmed up in any case.

**Dr. G. B. Mitchell-Heggs:** I disagree with Dr. Thorne; in these cases the desperate mother takes her child round from one hospital to another until she finds someone who will take action. In addition to this type of case, I feel that any in which vision is impaired, or feeding or excretion handicapped, should be watched. The distressed parents wonder whether their child is being properly fed or whether the ulcers which soon appear in the napkin region will heal, and travel in search of positive action. After a period of observation, if there is any increase in size, or no regression, I usually recommend appropriate radiotherapy and in certain cases, surgery.

**Dr. B. Bentley Phillips:** I have been treating these naevi for a number of years with thorium X paint, with a total of about 18 paintings. Whether it does a great amount of good I cannot say. I believe it obviates the trouble mentioned by Dr. Mitchell-Heggs in that it stops the parents taking the patients from one hospital to another. If no treatment is given the parents will continue to take the child round until they find someone enthusiastic enough to give treatment.

**Dr. D. I. Williams:** Some of us have seen cases treated elsewhere by radiation of unspecified amount with horrific, horrible sequelæ. These cases are so much in my mind that I am even more convinced it is best to leave these lesions alone.

**Dr. R. P. Warin:** In answer to the question whether the deep cavernous hæmangiomata continue whether if left untreated, I have followed up a series of cases for many years and all have cleared completely. In a number which have been left with overhanging skin I have wondered about advising plastic surgery but eventually they have flattened out without treatment. I am convinced that nothing we can do will improve on the final appearance obtained by leaving them untreated.

**Dr. G. C. Wells:** When we visited the Royal Sheffield Infirmary last year, Dr. H. Eckert and Professor G. M. Wilson showed us a girl with carcinoma of the thyroid gland which had resulted from X-ray treatment, given in early childhood for a capillary hæmangioma of the neck. Apparently the dose of X-ray had been quite small and it was not more than is commonly given by those who advocate radiotherapy for these lesions. Several such cases of carcinoma of the thyroid seem to have resulted from small doses of X-ray in childhood (Wilson *et al.*, 1958) and this may be another argument against using X-rays for capillary hæmangiomata.

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**Dr. Brian Russell:** I agree with Dr. Mitchell-Heggs' view that if the hæmangioma is likely to interfere with breathing, feeding, vision or defæcation, something should be done; otherwise not. I have never seen a child under school age who showed any serious emotional disturbance because of a simple hæmangioma. It is the mother who is anxious. As to X-ray treatment, I have seen a young woman with

non-development of one breast following X-ray treatment in infancy of a hæmangioma there—a lesion which would have disappeared if left alone. X-ray treatment should certainly not be used for lesions near the genitalia, on the breasts or over epiphyses.

**The President:** The consensus of opinion seems to be that each case must be treated on its merits, and that there is need for considerable discretion in the use of X-rays.

**Erythrodermia. Idiopathic Steatorrhea.**—BRIAN RUSSELL, M.D., F.R.C.P.

D. B., male, aged 27. Clerk.

**History.**—Thirteen years ago: Onset of weeping, scaly rash in front of right ear, spreading to involve the whole body within a few months. Eight years ago there was some response to T.A.B. while an in-patient at another hospital. Five years ago: Admitted to the London Hospital complaining of progressive weakness and pallor for seven months.

**Clinical findings.**—Pigmentation and exfoliation of skin. Sparse hair, ectropion and epiphora. Blood pressure 150/45.

**Investigations.**—Hæmoglobin 15%. Serum calcium 7.4, phosphorus 6.4 mg./100 ml. Acid phosphatase 0.6, alkaline phosphatase 10.0 K.-A. units. Total plasma proteins 6.0, albumin 3.9, globulin 2.1 grams/100 ml. Sternal marrow—megaloblastic erythropoiesis. Barium meal and follow through—steatorrhea pattern in small intestine.

He received blood, protein, vitamin and mineral replacements. The skin was treated with bland applications. The ectropion and epiphora have persisted and superficial corneal erosions have occurred, as well as an ulcer over the right medial malleolus.

There has been improvement in both the skin and general condition. The serum proteins, serum calcium, serum phosphorus, blood count and hæmoglobin are now normal.

**Dr. M. Garretts:** Professor C. E. Dent and I have studied two of his cases, and two cases of Dr. P. J. Hare's, suffering from hypocalcæmia associated with either widespread eczema, or with erythrodermia. In each case dramatic improvement occurred, often repeatedly, when the serum calcium was restored to normal either with vitamin D, or parathyroid hormone, or calcium gluconate injections. In this case of idiopathic steatorrhea the stage is set for hypocalcæmia to occur. It would be worth studying the calcium metabolism.

**The President:** Might this not be a reticulosis in the skin, with visceral involvement?

**Dr. Louis Forman:** The association between this type of erythrodermia and steatorrhea is by no means uncommon. I have seen light sensitivity with prurigo and much pigmentation associated with

faulty intestinal absorption indicated by an abnormal fat content of the stools. Liver extract by injection has led to considerable improvement. Dr. Garrett's contribution to the discussion suggests that further improvement might have resulted if more attention had been directed to the calcium blood levels.

**Dr. Brian Russell:** The serum proteins and the serum calcium were low and the serum phosphorus high when the patient was first seen. They are now within normal limits.

**Lupus Erythematosus. Polymyositis.**—WALLACE WHITE, M.B.

W. W., male, aged 52. Tailor.

**History.**—Forty-five years ago: Chilblains on hands in winter which remained as scars in summer.

Thirty years ago: Development of lupus erythematosus of face and forearms. Fingers became cold, numb and blue, especially in winter. Feet involved to a lesser extent.

Twelve years ago: Frequent attacks, especially in cold weather, of severe pain, tingling and burning in fingers. Similar involvement of ears, cheeks and nose. Movement of many interphalangeal joints diminished or absent. Lupus erythematosus improved with quinine and bismuth and Raynaud's attacks relieved by nicotinic acid.

Seven years ago: Exacerbation of lupus erythematosus controlled by mepacrine. Ulceration of fingers persistent.

Five years ago: Ulceration of fingers healed following treatment with chloroquine.

Nine months ago: Onset of weakness especially in legs. Losing weight.

Six months ago: Weakness of legs more marked. He had to help himself up from a chair.

**Clinical findings.**—Scarred atrophic pigmented and telangiectatic skin on the cheeks, nose, ears, hands, forearms and sternum. Partial or complete loss of nails. Changes typical of acrosclerosis present in the fingers.

There is generalized muscular wasting which is most marked in all muscle groups of the left thigh and, to a lesser extent, in the right thigh and both deltoids and triceps.

**Investigations.**—Electromyograph showed changes typical of polymyositis. E.S.R. (Westergren) 24 mm. in one hour. Plasma proteins: Total 7.7, albumin 4.4, globulin 3.3 g./100 ml. No L.E. cells seen.

**Comment.**—The occurrence of polymyositis with lupus erythematosus has been observed many times. Keil (1940) and Banks (1941) noted several cases showing a clinical transition from systemic lupus erythematosus to dermatomyositis. Klemperer *et al.* (1941) found inflammatory infiltrates in muscle in 5 of 30 cases

of lupus erythematosus. One case showed a striking polymyositis. Degos (1945) observed a phase of acute lupus erythematosus with Libman-Sacks endocarditis in a fatal case of dermatomyositis. Gougerot *et al.* (1947) observed that lupus erythematosus may closely resemble poikilodermatomyositis. This myasthenic form of lupus erythematosus has a raised electrical threshold and rapid fatigability of muscles.

Degos *et al.* (1949) found muscle biopsy and electromyographic findings typical of dermatomyositis in a case of subacute lupus erythematosus.

De Graciansky (1949, 1953) and Garcin *et al.* (1955) described cases in which, as in our case, there were long transitional periods of five to twenty years between the two phases of the illness.

Pagel and Treip (1955) observed further transitional cases and noted the constant occurrence of histological changes in the muscles, suprarenals and nail bed in both dermatomyositis and lupus erythematosus.

O'Leary *et al.* (1955) performed electromyography, skin and muscle biopsies on cases of lupus erythematosus and dermatomyositis. Electromyography showed diseased muscle in 20% of the former and in all the latter. The electromyogram was similar to that found in other active degenerative myopathies, unlike the neuritic type found in polyarteritis nodosa. The muscle shows degeneration, crowding of nuclei and motor end plate degeneration. There is perivascular lymphocytic infiltration and rarely eosinophils.

This picture resembles that found in myasthenia gravis and carcinomatous neuromyopathy and like them the condition may be improved by Tensilon.

Lees and Ferguson (1959) record a case of chronic atrophic dermatitis, chronic progressive myositis and coexisting subacute combined degeneration of the cord with defective vitamin-B<sub>12</sub> absorption.

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**Dr. R. H. Seville:** Why not diagnose this case as dermatomyositis? I showed a case in Manchester two years ago who was accepted as clinically looking like lupus erythematosus. She had had the symptom six years and died six months ago from breast carcinoma secondaries.

**Dr. P. Hall-Smith:** A case which was generally agreed as being lupus erythematosus, was shown at the Brighton B.M.A. meeting, 1956. It was then seen by the President, Dr. J. T. Ingram, who diagnosed dermatomyositis and suggested a chest X-ray, barium meal and follow through. These had already been done, but were repeated. A carcinoma of lung was discovered. On the other hand, in Dr. Wallace White's case I note the history of lupus erythematosus goes back thirty years; so I feel that a diagnosis of dermatomyositis can be ruled out here.

**Dr. Brian Russell:** The patient has responded to treatment for lupus erythematosus for thirty years whereas the muscular weakness and wasting have only been present for nine months.

**The President:** I would agree with the diagnosis of lupus erythematosus which may be associated with polymyositis. There is a relationship between lupus erythematosus and dermatomyositis but they do run their course as distinct entities. The only point with which I do not agree is that the changes in the fingers are typical of acrosclerosis. In my opinion that is not so. They are more typical of pustular psoriasis. It is important to recognize these separate entities.

The following cases were also shown:

**Ehlers-Danlos Syndrome.**—Dr. C. M. RIDLEY.

A patient shown at the Royal Society of Medicine by Dr. Parkes Weber in 1937 (*Proc. R. Soc. Med.*, 31, 553; Weber, F. P., and Aitken, J. H., 1938, *Lancet*, i, 198).

**Acanthosis Nigricans, Juvenile Type.**—Dr. BRIAN RUSSELL.

**Ectodermal Defect (Epidermolysis without Blister Formation).**—Dr. J. S. PEGUM.

**Chronic Erythema Multiforme.**—Dr. C. M. RIDLEY.

Woman aged 42; three years' history of ulcers of mouth, occasional rash elsewhere, clinically and histologically suggesting erythema multiforme; partially suppressed by steroids.

**Bullous Pemphigoid; Psoriasis; Hypertension.**—Dr. BRIAN RUSSELL.

The pemphigoid controlled by prednisone; both dermatoses controlled by triamcinolone.

**Pemphigus Foliaceus.**—Dr. J. S. PEGUM.

**Pemphigus Vulgaris; Osteomyelitis of Hand, following Steroid Therapy.**—Dr. BRIAN RUSSELL.

**Pemphigus Vulgaris.**—Dr. C. M. RIDLEY.

Onset at the age of 31 in a Jewish woman; maintained on steroids for three years.

**Hansen's Disease. Foot-drop. Tendon Transplant.**—Dr. BRIAN RUSSELL.

**Sarcoidosis: Lupus Pernio.**—Dr. J. S. PEGUM.

**Sarcoid following Wounds.**—Dr. PETER SMITH.

**Psoriasis showing Remission following Psychotherapy.**—Dr. JOHN COWIE.

**Pigmentation Due to Red Rubber Colostomy Belt.**—Dr. J. S. PEGUM.

**Atrophie Blanche.**—Dr. BRIAN RUSSELL.

**Atrophic Lichen Planus.**—Dr. WALLACE WHITE.

**Dermatomyositis.**—Dr. J. S. PEGUM.

**Urticaria Pigmentosa.**—Dr. J. S. PEGUM.

**Basal Cell Carcinoma Treated by Dermabrasion.**—Dr. C. M. RIDLEY.

Lesion on back confirmed by biopsy. Well twenty-one months later.

**Xanthomatosis; Xanthoma Tendinosum.**—Dr. N. A. THORNE.

A non-diabetic woman showing multiple nodules attached to tendons on hands, feet, elbows and knees. Considerable increase of serum cholesterol and serum lipids.

**Benign Familial Pemphigus.**—Dr. BRIAN RUSSELL.

**Cutaneous Granular Cell Myoblastoma.**—Dr. C. M. RIDLEY.

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## Clinical Section

President—Sir ERIC RICHES, M.C., M.S., F.R.C.S.

*Meeting*

March 13, 1959

**Myxædema, Goitre and Nerve Deafness in a Child**  
**Born in London.**—J. H. BURKINSHAW,  
M.R.C.P.

J. W., male, aged 20 months. Born 16.6.57.

*History.*—Well until October 1957 when he failed to make progress after severe whooping-cough. He had been noticed to suck poorly and had been gaining no weight for one month before the onset of the whooping-cough. While in hospital he took feeds poorly and gained only 2

smooth enlargement of the thyroid. Alert and interested in his surroundings, taking his feeds moderately well.

*Investigations* (December, 1957).—Serum cholesterol 300 mg. per 100 ml. No thyroxine or triiodothyronine detected in serum (Dr. J. H. Wilkinson, Westminster Hospital).

*X-rays* (aged 7 months): No delay in centres of ossification.



FIG. 1.—Aged 8 months. Showing myxædematous appearance.

oz. He was constipated. His appearance and history suggested hypothyroidism but the diagnosis was doubted because of his unusually bright and active behaviour.

*Family history.*—Father, from Radom, Poland (a non-goitrous area). Mother, English (from Twickenham). Brother aged 5: well, no goitre, not deaf. Paternal aunt is said to have a goitre but details have not been obtained as she is in Poland.

*On examination.*—November, 1957: Myxædematous-looking child, with easily palpable,



FIG. 2.—Aged 18 months. Showing normal appearance after thyroid treatment.

*Treatment.*—Thyroid treatment started in February, 1958— $\frac{1}{4}$  gr. daily gradually increased to  $\frac{1}{2}$  gr. b.d. Considerable improvement in appetite and appearance (Figs. 1 and 2).

Goitre has almost disappeared. January 1958—the mother noticed he was deaf. Deafness confirmed and diagnosed by Mr. F. Boyes Korkis as nerve deafness.

*Comment.*—The combination of myxædema, goitre and nerve deafness, though common in some endemic areas, has not been reported in other parts of the world.

**Spontaneous Rupture of the Œsophagus Secondary to Stricture.**—PAUL T. SAVAGE, F.R.C.S.

Mr. C. S., aged 44.

*History.*—Ever since childhood, he has noticed that food occasionally seemed to stick in the centre of his chest, but usually passed on down after drinking some water.

Three hours before admission, while eating his Sunday lunch, a piece of meat seemed to "lodge half-way down". He tried drinking some water, but this failed to dislodge it. He then tried drinking a hot cup of tea very quickly, and developed a sudden very severe retrosternal pain, which soon became agonizing. He was seen by his doctor, who gave him 100 mg. of pethidine

*Progress and treatment.*—Emergency operation (five hours after admission): Right lateral thoracotomy through the bed of the 7th rib, which was excised from the angle to costal cartilage. 4 oz. of dirty brown fluid were found in the right pleural cavity. The right posterior mediastinal pleura was seen to be intact, but bulged into the pleural cavity. Bubbles of gas were seen deep to the pleura. The posterior mediastinal pleura was opened from the arch of the azygos vein to the diaphragm and some dirty brown fluid removed, together with a piece of meat  $1\frac{1}{4} \times 1 \times \frac{3}{4}$  in. A longitudinal tear in the right lateral wall of the Œsophagus  $1\frac{1}{2}$  in. in length was then found. On passing a finger through this into the Œsophagus, a diaphragmatic stric-

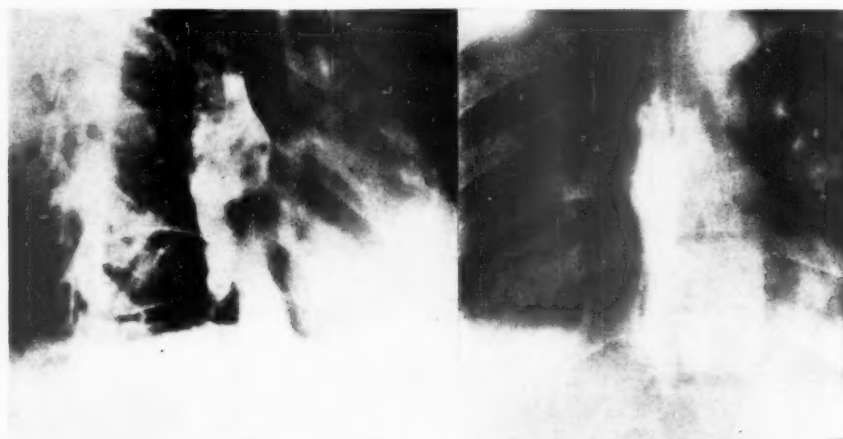


FIG. 1.—Diodone swallow: right anterior oblique and A.P. views, showing extravasation of diodone from right side of mid-Œsophagus, into posterior mediastinum.

intramuscularly, and admitted him to the Whittington Hospital, as an emergency.

*Physical examination and investigation.*—Ill-looking man of 44 in considerable pain, sweating profusely. Blood pressure 150/100. Slight tenderness and rigidity in upper abdomen but no other abnormal physical signs. X-ray of chest (A.P. and lateral): No surgical emphysema of mediastinum. X-ray of abdomen: No gas under diaphragm. E.C.G. normal; no evidence of myocardial infarction. Diodone swallow shows extravasation of contrast medium from the mid-Œsophagus into the right side of the posterior mediastinum (Fig. 1).

ture the size of a pencil was found just below the lower end of the rent. It was easily dilated. The rent in the Œsophagus was closed in two layers with interrupted 00 silk sutures, and the chest closed after inserting anterior apical and posterior basal intercostal under-water seal drains.

*Convalescence.*—The right lung remained completely expanded, but indigo-carmin given by mouth on the fifth post-operative day promptly appeared in the drainage tube. On the eighth post-operative day the nasogastric feeding tube was replaced by a gastrostomy, and within a few days the Œsophagocutaneous fistula healed. Further convalescence was uneventful.

# Four Cases of Sporadic Goitre and Congenital Deafness.—G. R. FRASER, M.B.<sup>1</sup>

- I. L. C., female, born 1948.  
 II. R. S., female, born 1904  
 III. E. N., female, born 1905 } sisters  
 IV. A. E., male, born 1899.

These 4 patients have in common congenital nerve deafness particularly in the upper frequencies (Table I) and a goitre coming on in late childhood. This goitre tends to recur after partial

TABLE I

Case	% of radioactive iodine trapped at 1 hour discharged by 400 mg. KClO <sub>4</sub>	Loss of hearing in decibels (average of the two ears)	
		256 cycles	2048 cycles
I	42	60	80
II	79	80	100+
III	43	75	100+
IV	66	100+	100+

thyroidectomy (as in Cases II, III, and IV), but responds to treatment with thyroxine which has recently been instituted in all 4 cases. In Case I the response has been so gratifying that thyroidectomy will probably be unnecessary.

It is thought that the goitre results from a block in the synthesis of thyroxine since potassium perchlorate given one hour after a dose of radioactive iodide discharges a variable amount from the thyroid gland showing that trapped iodide has not been incorporated into organic form (Table I). This block and the consequent underproduction of thyroxine causes increased secretion of T.S.H. from the pituitary and goitre formation.

This compensatory mechanism is sufficient to maintain most cases of this syndrome in a euthyroid state and in fact the mental and physical development of these 4 cases is normal.

From family studies it seems that this defect is inherited in a simple recessive manner. Cases II and III are sisters and their parents were first cousins. Case IV has 2 affected sisters and the family was described first by Brain (1927). In the families we have studied various degrees of nerve deafness always accompanied the goitre. It is not known how the two are connected though they are both presumably the effects of a single abnormal gene. The deafness is not due to hypothyroidism since the patients are euthyroid nor is there evidence that a fault in embryological development could pick out the thyroid and the auditory apparatus in this fashion. One possibility is that products of a deviant metabolic pathway poison the enzyme responsible for the oxidation of iodide to iodine and at the same time cause a toxic nerve deafness.

<sup>1</sup>Holder of a Medical Research Council Scholarship at the Galton Laboratory, University College, London.

Morgans and Trotter (1958) have already described 2 sibs with an identical syndrome. It may well be that these cases are intimately connected with familial goitrous cretinism of the type originally described by Stanbury and Hedge (1950). In this family the parents of the four affected sibs are first cousins and a discharge with potassium thiocyanate (which acts in the same way as perchlorate) is present. Their speech defect may well be due to undetected deafness.

These patients are included in a larger series which has been studied with Dr. M. E. Morgans and Dr. W. R. Trotter at University College Hospital.

We are grateful to Dr. A. D. M. Jackson and Professor A. A. Moncrieff for referring Case I and to Dr. A. Stuart Mason for referring Case II.

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# Behcet's Syndrome Complicated by Intracranial Thrombophlebitis.—H. C. MASHETER, M.B. (for T. PARKINSON, M.D., M.R.C.P.).

E. M., male, aged 29. Motor assembler.

**History.**—March 1958: Pain and stiffness in right elbow. Aspirated and treated with intra-articular prednisolone. July 1958: Effusion right knee similarly treated (diagnosis of ? rheumatoid arthritis made). Three weeks before admission he developed headaches and neck stiffness which gradually got worse. At the same time he noticed genital ulceration which persisted until admission. 10.10.58: Admitted to Luton and Dunstable Hospital with a three-day history of sore throat. Swallowing had been painful but not impossible and his voice was hoarse.

**On admission.**—Temperature 99.4° F. Shallow ulcers of scrotum and old healed lesions; similar lesions of uvula; psoriasis both elbows and no limitation in any joints except the cervical spine. C.N.S.: Equivocal left VII nerve weakness. No papilloedema. No signs of meningitis.

**Investigations.**—E.S.R. (Westergren) 90 mm. in first hour; Hb 71%; throat swab *Strep. viridans*; swab from genital ulcer, coliform bacilli, faecal streptococci and micrococci; Rose-Waaler negative; chest X-ray normal. Blood W.R. negative.

**Progress and treatment.**—At this stage, a clinical diagnosis of Behcet's disease was made, and an intensive course of prednisolone was given, commencing at 40 mg. per day, the course

being tailed off and finished after eighteen days. Good response; patient's headache became less severe; ulceration of uvula healed in one week and of scrotum in four weeks. Allowed home 30.10.58. One week after corticosteroids stopped, patient developed severe frontal headache and neck stiffness and for the first time began to vomit daily. When reviewed in Out-patients (14.11.58) there was now present bilateral papilloedema. All neck movements grossly limited, especially flexion. Kernig's sign negative. Otherwise C.N.S. normal. E.S.R. 92 mm.; Hb 69%. Skull and chest X-rays (repeat) showed no abnormality.

Because of severe papilloedema, he was transferred to a neurosurgical unit under Mr. J. E. A. O'Connell and ventriculograms were done. Intra-ventricular pressure was raised but X-ray patterns of ventricular systems were normal. Ventricular C.S.F.: No pus or inflammatory cells. Intracranial thrombophlebitis of a dural sinus was diagnosed. Transferred back to Luton and Dunstable Hospital and daily lumbar punctures effected good reduction of C.S.F. pressure from 300 mm. There were now severe headache and nystagmus to right and left. There was gradual improvement and three weeks later neurological examination was normal except for the presence of bilateral papilloedema. Anticoagulant therapy was commenced to prevent further thrombosis and progress has been entirely satisfactory. His headache has almost gone, papilloedema is less marked and no oro-genital ulceration is present. Visual acuity 6/9 right and 6/12 left. His healed ulcers of scrotum are still to be seen but his joints are normal.

*Comment.*—Behcet's syndrome or disease is endemic in the Eastern Mediterranean basin and was probably first described by Hippocrates. Feigenbaum (1956) thought that Hippocrates' description in the Third Book of Endemic Diseases was similar to that made by Behcet in 1937.

The Behcet triad consists of relapsing iritis and oral and genital ulceration, although in many cases the iritis tends to appear later. The condition may also be manifest as arthralgia, thrombophlebitis, neurological and skin lesions. The present case fulfils the criteria of Behcet's disease in that the patient had both oral and genital ulceration and also arthritis. He had no eye lesions but Curth (1946) considered that the diagnosis could be made without them. He presented with arthritis some six months before oral and genital ulceration. He also had mild psoriasis and at different stages of his illness it was thought that he had either rheumatoid arthritis or psoriasis arthropathica. The disease was complicated by otitic hydrocephalus which came on approxi-

mately one month after treatment with corticosteroids. He had typical findings of this condition, namely papilloedema, normal-sized ventricles, raised C.S.F. pressure and normal cytology of C.S.F. According to Sir Charles Symonds (1956) this indicates that thrombophlebitis has occurred in a dural sinus.

Thrombophlebitis is a well-recognized complication of Behcet's disease and France *et al.* (1951) report that 27.3% of cases suffered from thrombophlebitis. These episodes tended to be multiple, and involved sites as varied as subcutaneously in the legs, retinae and inferior vena cava. C.N.S. involvement occurred in 10% of cases but this patient did not show a clinical picture at all similar to that described by Evans *et al.* (1957), McMenemy and Lawrence (1957), Williams (1958) and Phillips and Scott (1955) where C.N.S. involvement was thought or proved at post-mortem to have occurred.

*Summary.*—This patient shows the Behcet syndrome without eye lesions. He presented unusually with polyarthritis six months before his ulcers appeared and his disease has been complicated by thrombophlebitis in an uncommon site, namely a dural sinus, giving rise to otitic hydrocephalus.

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The following case history was presented:

**Hæmorrhagic Pericardial Effusion (? Tuberculous) in an African.**—Dr. F. M. PURCELL.

The following cases were also shown:

**Polymyositis with Pneumoconiosis.**—Dr. A. W. JOHNSTON (for Dr. M. ASHBY).

**Marfan's Syndrome with Aortic Incompetence.**—Dr. J. LISTER.

**Megacolon.**—Dr. J. W. MACK (for Miss M. WATERFALL).

**Multiple Congenital Arteriovenous Fistulae of Left Leg. Avascular Necrosis of Left Tibial Epiphysis.**—Mr. B. LYTTON (for Mr. H. TAYLOR).

Meeting  
May 8, 1959

MEETING HELD AT THE SOUTHBEND GENERAL HOSPITAL

## Ulcerative Colitis Treated by Total Colectomy and Ileorectal Anastomosis (I.R.A.)

By H. GORDON UNGLEY, F.R.C.S.

London

4 patients (all working) were shown as representative of a group of severe cases of ulcerative colitis treated by total colectomy and I.R.A.

*Case I.*—Mr. G., born 1929. Duration of symptoms eight months. Proctocolitis with repeated severe hæmorrhages. Total colectomy and I.R.A. in one stage, November 1953. Bowels open three to four times a day; no blood. Rectum normal.

*Case II.*—Mr. B., born 1910. Duration of symptoms one year. Severe proctocolitis with pseudopolyps and strictures to anus. Two-stage operation: July 1953—Total colectomy (see Fig. 1) and ileostomy. February 1954—I.R.A. Patient passes finger *per rectum* alternate days. No stricture. Bowels open five to six times daily. Nil at night. No blood.

*Case III.*—Mr. T., born 1921. Duration of symptoms one year. Severe proctocolitis with bleeding and loss of 4 st. in weight. One-stage total colectomy and I.R.A., October 1957. Bowels open three times a day; no blood. Regained 4 st.

*Case IV.*—Mr. S., born 1903. Duration of symptoms nine years. Severe proctocolitis with rectal stricture. One-stage total colectomy and I.R.A., October 1957. Bowels open eight times in twenty-four hours.

Medical treatment is always employed in ulcerative colitis and frequently controls the condition but in about 25% surgery is required. These are the most important indications:

(1) Failure of medical treatment to keep the

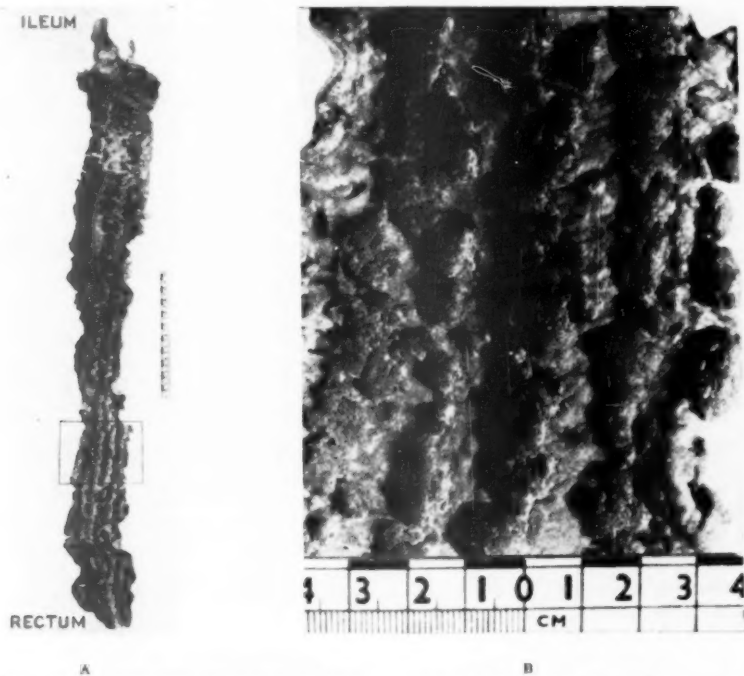


FIG. 1 (*Case II*).—A, The colon together with the appendix and a few inches of the ileum. The dark areas are granulation tissue over ulcers. The disease extended to the whole of the rectum which was involved as severely as the colon. B, Enlarged view of area outlined in A.

patient fit enough to live a normal life. For example, to avoid repeated hospitalization, chronic ill-health and malnutrition (Case III) or when an acute case fails to respond to medical treatment.

(2) The danger of malignant disease following chronic ulceration. This danger has been emphasized by many writers abroad, particularly in the United States. It has been perhaps overstressed, but when the disease has been present for more than ten years, everyone would agree that a scarred, ulcerated or strictured colon is a potential danger to the patient and better removed. This does not refer to the mild forms of the disease with only slight changes in the bowel.

(3) In fulminating cases when the patient's condition is deteriorating under medical treatment. In these patients surgery is an urgent emergency measure with ileostomy (preferably with total colectomy) as the first stage.

(4) The complications of hæmorrhage (Case I), perforation, pericolic abscess (Case IV) and obstruction (for example by stricture) are clear and often urgent indications for operation.

Once it has been decided that surgery is necessary all agree that total colectomy is an essential part of the operation. We can now discuss the indications and contraindications for ileorectal anastomosis (I.R.A.), compared with total proctocolectomy and permanent ileostomy.

There is, it is true, a weight of opinion in America and in the United Kingdom towards proctocolectomy, but at the Gordon Hospital, where we have 700 cases under observation, we differ from this view. When we speak of surgery for ulcerative colitis, we mean total colectomy and I.R.A. It is quite exceptional for us to leave a permanent ileostomy—in fact, out of some 175 patients submitted to total colectomy, it has been necessary to remove the rectum in only 7.

The operation entails the removal of the whole colon. The rectum is divided through its upper third. The ileum is anastomosed to the rectum where this is covered by peritoneum anteriorly, i.e. its middle third. The remaining rectum is, therefore, about 10 cm. in length. In severe cases with a heavily infected rectum the operation is performed in two stages: first, a total colectomy with ileostomy, then an anastomosis of the ileum to the rectum. The interval between these two stages varies from a few weeks to two years.

#### INDICATIONS FOR REMOVAL OF THE RECTUM

Removal of the rectum may be necessary for the following reasons:

*Fistulae.*—In the past, patients with fistula-in-ano have been considered unsuitable for I.R.A. but, in our experience, the majority of fistulae heal after total colectomy and ileostomy and these patients have been successfully treated by a second stage anastomosis. On occasions a high fistula-in-ano or a rectovaginal fistula may fail to heal after the colectomy which is an indication for a second-stage abdomino-perineal excision of the rectum.

An example of such a case, where removal of the rectum was required, was a woman of 67 years with multiple fistulae around the anus and widespread skin necrosis. She was also incontinent. When lying on her side the anal canal was so patulous that the ampulla of the rectum was in full view when the buttock was lifted. After total colectomy in 1955 she gained several stones in weight, but her rectal control did not improve with physiotherapy. Here I did not feel justified in making an anastomosis and so I removed the rectum. She remains well and is now 71 years old.

*Malignant disease.*—We all recognize the possibility of malignant disease developing in the colon or rectum in these patients, particularly when the disease has been present for ten years or more, but it is satisfactory to record that even a severely inflamed rectum with pseudo-polyps (Cases III and IV) and strictures (Case II) can return to normal or near-normal after a colectomy and anastomosis. We have patients in whom an anastomosis has been functioning for twelve years and whose rectums remain healthy. A young patient with more than ten years' severe disease should be considered as a probable candidate for proctocolectomy unless the rectum has never been severely inflamed.

*Contracted rectum.*—Fibrous stricture of the rectum has been regarded as a contraindication but we have found that most strictures can be dilated and the rectum thus made suitable for anastomosis. Even a shrivelled rectum, which will not admit a finger, can be gradually dilated to a calibre which permits a second-stage I.R.A. and normal bowel actions (Abel, 1959). In exceptional cases the rectum is beyond such treatment and is a danger to the patient. In only one case (with a ten-year history) have I been obliged to remove the rectum on account of stenosis.

#### SEVERE RECTAL INVOLVEMENT

It is quite untrue to say that a rectum which is severely involved by disease, showing pseudo-polyps or stricture, is unsuitable for I.R.A. All

of us who practise this method (Aylett, 1959, reported 100 cases of colitis treated by this technique) have seen patients with severe proctitis in whom the rectum has become normal after total colectomy and ileostomy and in whom anastomosis has been successfully performed. The interval between the colectomy and the "hook-up" varies from a few weeks to many months. Case II had severe proctocolitis (see Fig. 1) with pseudo-polyps and stricture extending to the anus. A total colectomy and ileostomy was performed in July 1953. Daily dilatation and irrigation of the rectal stump gradually restored its lumen and the anastomosis was performed in February 1954. He remains well.

In conclusion, therefore, though we admit the need for total proctocolectomy in exceptional cases, we feel that for most patients the most rational surgical treatment is total colectomy and ileorectal anastomosis in one or two stages. We know that a diseased rectum can heal, pseudo-polyps disappear, strictures be controlled and fistulae close.

Ileorectal anastomosis is therefore indicated for all patients requiring surgery, with only the few exceptions we have mentioned.

*Acknowledgment.*—I am pleased to record my thanks to Dr. Ian Dawson, Department of Pathology, Gordon Hospital, and to Dr. Peter Hansell, Department of Photography, The Westminster Hospital, for their help with the illustration.

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**Subdural Hæmatoma.**—T. ROWLAND HILL, M.D.  
W. S., female, aged 47 years.

Seven weeks before admission she started vomiting and complained of daily headaches. The headaches were worse in the mornings, frontal and occipital in distribution, variable in duration and worse on sitting up. She developed vertigo, especially on standing, and tinnitus, worse on the left side. The fortnight before admission she grew much worse, developing left-sided deafness and complaining of diplopia, especially to the left.

Her general condition was sound, there was no atherosclerosis or hypertension. She showed conjugate ocular palsies, pronounced on gazing upward, with weakness of lateral conjugate movements. There was partial right ptosis. There were no other neurological signs.

Lumbar puncture showed clear cerebrospinal fluid under such low pressure that it had to be withdrawn with a syringe. The total protein was 66 mg.%. No pleocytosis; W.R. negative.

The usual exploratory burr holes were made (Mr. Ian McCaul) and bilateral subdural hæmatomata drained. It took some time for the brain to re-expand (see Fig. 1) but eventually full recovery took place and the patient has remained quite well.

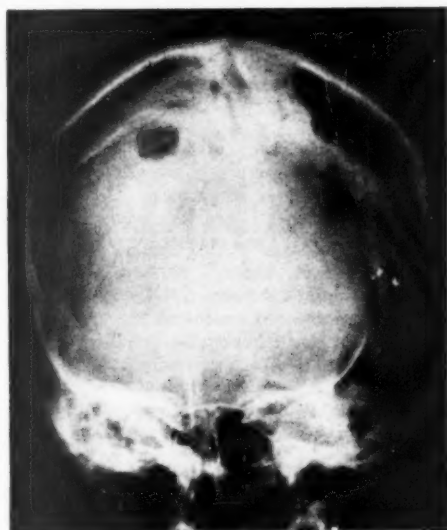


FIG. 1.—Bilateral subdural hæmatomata, showing the hæmatomata replaced by air and the cerebral hemispheres not yet expanded.

*Comment.*—The point of interest in this case is the virtually spontaneous development of bilateral subdural hæmatomata in a healthy woman with no signs of atherosclerosis or old age. The only evidence of past head injury that could be elicited was that she had hit her head, not very hard, on the corner of a kitchen cupboard three months previously. The other point of interest is the development of "false localising signs", i.e. progressive deafness and conjugate ocular palsies which suggested a brain-stem lesion such as neoplasm. These were due to pressure on the brain stem from above through the tentorium.

All these signs and symptoms disappeared after drainage.

**Subarachnoid Hæmorrhage (Three Cases).**—T. ROWLAND HILL, M.D.

I.—J. C., female, aged 30 years.

A fortnight before admission, while playing the piano, she developed a sudden occipital headache and felt slight "pins and needles" in the left arm and foot. She rested in bed and recovered

slowly till a fortnight later, when, while resting quietly, she suddenly felt a severe occipital and right parietal headache, with a stiff neck.

A few hours later there was a sudden increase in pain, she vomited and noticed she could not see to the left (left homonymous hemianopia).

*On admission.*—Neck rigidity, left homonymous hemianopia and left extensor plantar response. The C.S.F. was under high pressure and was heavily blood-stained. It was decided to ligate the right common carotid artery as an emergency.

Within a few hours of ligation the plantars were both flexor and the homonymous hemianopia had completely disappeared. She rapidly made a full recovery and has been back at a normal working life as a teacher for several years.

*Comment.*—The interest of this case lies in the successful emergency treatment by carotid ligation that often saves lives in this condition.

Each case of subarachnoid haemorrhage should be judged on its merits. To rely too much upon statistical data for prognosis and treatment is dangerous. Many leaking intracranial aneurysms lie near enough to the anterior part of the circle of Willis for carotid ligation to reduce the force of systole enough to stop further bleeding.

Another point of interest is the rapid disappearance of focal signs after ligation. The hemianopia completely and rapidly vanished. This has often been observed and it must be assumed that an enlarging and leaking aneurysm somehow impairs the cerebral circulation above it, perhaps by provoking vasospasm.

II.—A. D., male, aged 41 years.

Three days before admission this man developed sudden "bursting" headache which came on in the afternoon and persisted till his admission when he had been unconscious for one hour.

*On examination* he had marked neck stiffness and a right external rectus palsy. The general condition was good with no atherosclerosis or hypertension. Left plantar extensor. The cerebrospinal fluid was under raised pressure and was heavily blood-stained.

Twenty hours after admission, although resting in bed, he developed increased headache and became restless. Neck stiffness was more pronounced. It was clear that a second haemorrhage was occurring and his right common carotid, after being compressed for twenty minutes without hemiparesis, was immediately ligated.

Preliminary carotid compression was done in all these cases.

After ligation no further deterioration was observed but two days later the right VI nerve palsy was less pronounced. Six days later there was no overt strabismus and only occasional diplopia. Three weeks after admission he was discharged, well and symptomless, and he has led a normal working life and remained well for the last four years.

*Comment.*—This is another example of the use of common carotid ligation as a simple life-saving measure in a case of recurrent subarachnoid haemorrhage. The right VI nerve palsy suggested an internal carotid artery aneurysm, or one very nearby and thus likely to be favourably affected by carotid ligation. Delays in transfer to a neurosurgical centre, in the performance of angiography and in considering the major procedure of direct surgical approach must be set against the speed, simplicity and effectiveness of the ligation procedure in the right cases.

III.—A. W., female, aged 72 years.

While doing housework four days before admission to hospital she suffered sudden occipital headache. She vomited and the headache persisted. There was considerable atherosclerosis and the blood pressure was 250/120. There was much neck-stiffness on admission. Deep reflexes were slightly increased on the left side. The cerebrospinal fluid was heavily blood-stained but not under increased pressure. The headache persisted and three days after admission she became drowsier with conjugate deviation of the eyes to the right and a left hemiparesis. Her condition continued to deteriorate and clearly a second haemorrhage was taking place.

Six days after admission ligation of the right common carotid artery was therefore carried out.

Twenty-four hours later there was a distinct improvement in the level of consciousness and the hemiplegia. Her headache rapidly lessened. She has remained quite well, leading an active life and walking well. She uses her left hand quite well despite the slight left hemiparesis that remains.

*Comment.*—This case illustrates that life-saving carotid ligation is possible without side-effects in elderly, atherosclerotic patients. It also shows how a hemiplegia caused by subarachnoid haemorrhage can sometimes show dramatic improvement immediately after carotid ligation, for the presumed reasons given in Case I.

**Chronic Beryllium Poisoning (Two Cases).—E. G. SITA-LUMSDEN, M.D., M.R.C.P.**

I.—Mr. L. B., aged 44, was found to have finely granular and mottled opacities throughout both lungs when examined by a mass radiography unit in April 1957. He was well and there were no abnormal signs. From 1945–50 he had been foreman in charge of the preparation of a zinc-beryllium-manganese silicate powder in a fluorescent-lamp factory. The material contained about 5% of beryllium oxide. He was negative to 100 units Old Tuberculin. Serum proteins: total 6.1, albumin 2.2, globulin 3.9 g./100 ml. E.S.R. 9 mm. in the first hour (Westergren). Beryllium patch tests strongly positive. Urine negative for beryllium. By October 1958 he complained of loss of weight (22½ lb. in the previous twelve months), lassitude, anorexia, cough and exertional dyspnoea. Crepitations were audible throughout both lungs, and there were signs of right heart strain. The X-ray film showed progressive fibrosis and the E.S.R. had risen to 25. Lung function studies (Dr. L. H. Capel) showed a vital capacity of 61% of expected value, the forced expiratory volume at 1 second being 76% of the vital capacity. Diffusion of CO was less than half normal. Treatment was started on 17.10.58 with prednisolone 20 mg. daily for three months, followed by 10 mg. daily to date. Improvement was rapid with disappearance of cough and dyspnoea and gain in weight. The E.S.R. fell to 4, but the serum proteins remained abnormal. He remained tuberculin-negative, while the beryllium skin tests gave weaker reactions. The X-ray films have shown little change, with slight clearing only of the finer granularity. Lung function tests show an improvement in his ventilation but no significant decrease in the degree of alveolo-capillary block.

II.—Mr. J. E., aged 51, was seen in April 1958 with a six-months history of cough, dyspnoea and loss of weight (10 lb. in past year). He was slightly cyanosed and a little dyspnoeic on exertion, and the breath sounds were diminished. Chest X-ray film showed mottling throughout both lung fields, with thickening of the lesser fissure, basal emphysema and slight enlargement of the hilar nodes. Tuberculin-negative to 100 units Old Tuberculin, E.S.R. 27, beryllium patch tests strongly positive. Urine negative for beryllium. From 1942 to 1950 as research chemist he had been supervising the manufacture of the beryllium-phosphor to which Case I was exposed. By September 1958 he had deteriorated with increasing cough, sputum, dyspnoea and lassitude, and had lost a further 10 lb. Crepitations were present in both lungs and the E.S.R. had risen to 38, but the X-ray film showed no change. Treatment was

started on 16.9.58 with prednisolone 20 mg. daily for eight weeks. It was then tailed off and stopped on 17.3.59. Improvement was again rapid and complete and in this case there was much greater clearing of the X-ray appearances, leaving only slight streaky shadowing. Lung function tests showed a slight improvement in the ventilatory capacity but a severe alveolo-capillary block persists. Since treatment was stopped there has been a gradual return of fine mottling in the lungs, but the patient remains well.

**Argentaffinoma of Ileum, Causing Obstruction.**  
H. GORDON UNGLEY, F.R.C.S.

A woman aged 90, with four years of irregular bowel action diagnosed as diverticulitis of sigmoid (confirmed by X-ray), developed intestinal obstruction which was incorrectly attributed to the diverticulitis. At operation (November 1958) stricture and multiple adhesions of the terminal ileum, with massive lymphadenopathy, proved to be the cause of the obstruction. Resection of 3 ft. of ileum, with adjacent glands, was followed by recovery. The diverticulitis was confirmed but was not disturbed.

**Urinary HIAA excretion.**—9.4 mg. in 900 ml. on November 16–17, 1958, 21 mg. in 670 ml. on December 1–2, 1958 (normal excretion 2–10 mg. in twenty-four hours).

**Wandering Spleen.**—H. GORDON UNGLEY, F.R.C.S.

A woman, aged 46, with three years' persistent mild upper abdominal discomfort. Firm tumour movable from right to left of umbilicus.

March 1959: Laparotomy revealed a normal spleen with a 25 cm. pedicle. The colon was also on long mesentery from caecum to sigmoid. After splenectomy, pathological examination showed a normal spleen. Recovery. Blood count one month later normal.

**Oesophagectomy via Split Sternum Approach**  
(Moore, 1955).—H. GORDON UNGLEY, F.R.C.S.

Man, aged 54.

**Operation** (May 1957): After a left upper paramedian laparotomy, the incision was extended upwards in the mid-line to level of the 4th costal cartilage. Sternum was split with Lebsche chisel (about 5 cm. of bone being divided). A right submammary incision was made to mid-axilla down to the 4th cartilage and rib. Pleura opened across bed of rib and after ligating internal mammary vessels, the small right section of the sternum was divided. A spreader was used to separate the ribs and the mid-line wound. A growth at the junction of the middle and lower third of the oesophagus

was resected and œsophagus anastomosed to the closed mid-body of stomach (May 1957).

*Pathological report.*—"The specimen consists partly of œsophagus and partly of stomach. The two form a tube 15 cm. long. The upper end of the specimen consists of œsophagus 2 cm. long. At the junction of œsophagus with stomach mucosa there is a malignant ulcer 1 cm. long which encircles the whole of the lumen. No lymph nodes are present in the adjacent soft tissues. *Conclusion.*—Adenocarcinoma of the stomach with short œsophagus".

He remains well two years following operation.

*Comment.*—An excellent exposure though perhaps more traumatic than the usual laparotomy and right thoracotomy.

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The following cases were also shown:

- (1) **Adenoma of Stomach.** (2) **Malignant Tumour in an Undescended Testicle.**—Mr. R. WALKER BRASH.

- (1) **Cor Biloculare.** (2) **Uræmic Ulceration of Small Intestine.** (3) **Spontaneous Rupture of Spleen.** (4) **Pseudomyxoma Peritonei.**—Dr. S. J. BEALES.

**Unilateral Aphakia Corrected by Anterior Chamber Acrylic Implants.**—Mr. D. P. CHOYCE. (See *Trans. ophthal. Soc. U.K.*, 1958, 78, 459; *Lancet*, 1958, ii, 196; *Amer. J. Ophthalm.*, 1959, 57, 253, 254.)

- (1) **Cirroid Aneurysm of Scalp.** (2) **Multiple Carcinoma of Large Gut.**—Mr. R. W. WEINBURG.

- (1) **Hæmolytic Anæmia.** (2) **Portal Systemic Encephalopathy.**—Dr. J. C. COURY.

- (1) **Multiple Salivary Gland Enlargement.** (2) **Hamatoporphyrinuria.** (3) **Prednisolone-treated Nephrosis.** (4) **Recurrent Spontaneous Pneumothorax Treated by Pleurectomy.**—Dr. R. SLEIGH JOHNSON.

**Prosthetic Replacements of Femoral Head.**—Mr. D. L. EVANS.

**Arteriovenous Aneurysm.**—Mr. A. G. DINGLEY.

**Pelvic Thyroid Causing Thyrotoxicosis.**—Miss E. M. WHAPHAM and Dr. D. C. CALDWELL.

**Lymphatic Obstruction Following upon Radical Mastectomy.**—Mr. DONALD BARLOW.

**Diverticulum at Lower End of Œsophagus.**—Mr. B. J. SANGER.

- (1) **Hashimoto's Disease.** (2) **Fibrosarcoma of Thigh.** (3) **Carcinoma of Scrotum.**—Mr. ANDREW MONRO.

- (1) **Carcinoma of Duodenum.** (2) **Primary Amyloidosis.**—Dr. R. G. BENIANS.

**Fibrocystic Disease of Pancreas.**—Dr. R. H. DOBBS.

**Addison's Disease in Pregnancy.**—Mrs. F. BRIDGE.

**Ulnar Nerve Palsy due to Ganglion of Wrist.**—Mr. JOHN SHELSWELL.

The following papers were also read:

**Results of 118 Cases of Bilateral Adrenalectomy and Oophorectomy.**—Mr. DONALD BARLOW.

**Fibrocystic Disease of the Pancreas.**—Dr. R. H. DOBBS.

**Argentaffinoma of Small Intestine.**—Mr. H. GORDON UNGLEY.

**Chronic Berylliosis of the Lungs Treated with Corticosteroids.**—Dr. E. G. SITA-LUMSDEN.

**Salivary Gland Enlargement.**—Dr. R. SLEIGH JOHNSON.

Dr. K. M. PACKETT and Dr. D. F. REYNOLDS showed X-ray films, including:

- (1) **Metastatic Carcinoma of the Œsophagus.** (2) **Neurofibromatosis of the Colon.** (3) **Retroperitoneal Air following Colonic Perforations.** (4) **Osteomyelitis of the Spine Presenting with Pleural Effusion.** (5) **Benign Synovioma Indenting a Terminal Phalanx.**

Mr. DONALD BARLOW showed a film of **Bilateral Adrenalectomy and Oophorectomy Through a Single Incision.**

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# **Cedilanid**

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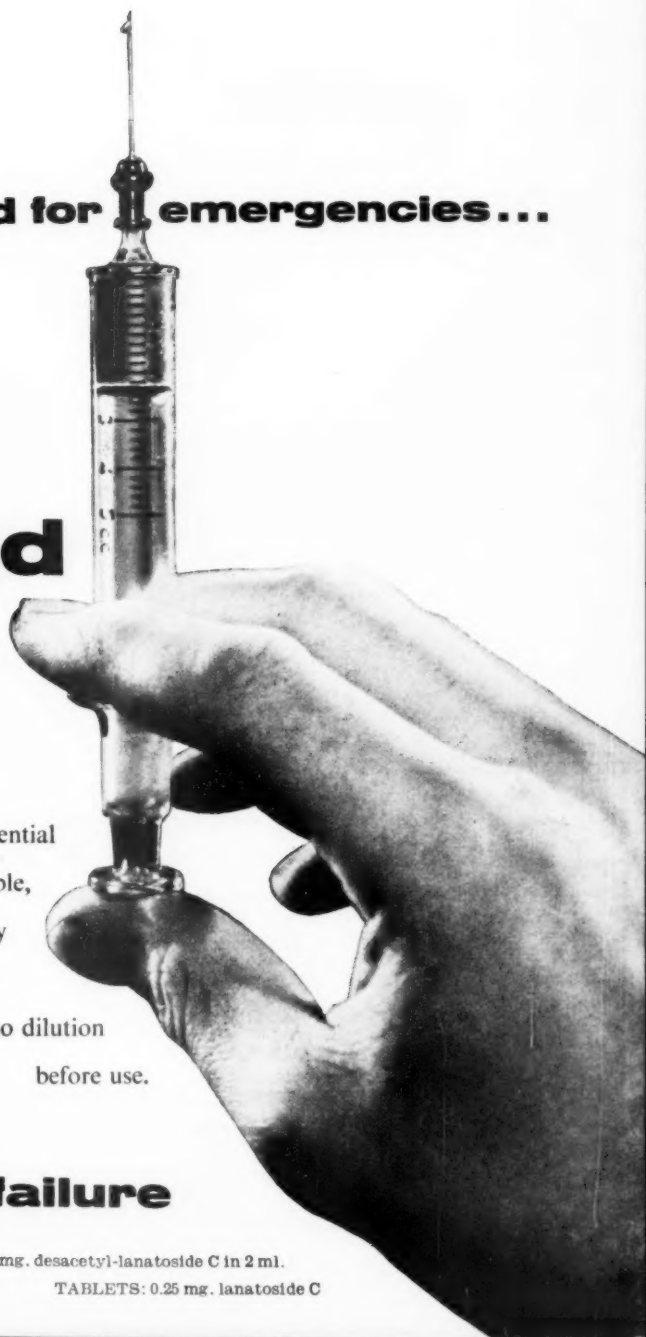
When emergency digitalisation is essential  
and the intravenous route impracticable,  
Cedilanid may be given intramuscularly  
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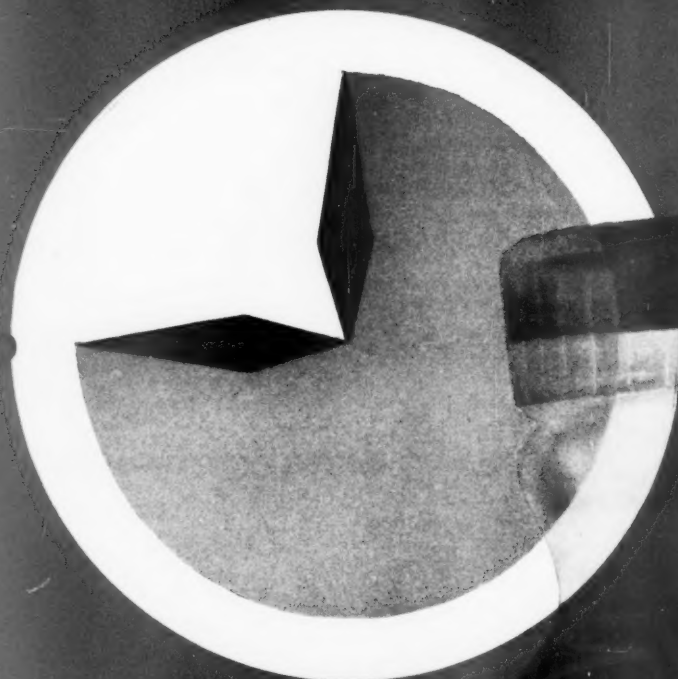
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## Section of Endocrinology

President—Professor F. T. G. PRUNTY, M.D., F.R.C.P.

Meeting  
May 27, 1959

### Primate Growth Hormone Studies in Man [Summary]

By JOHN C. BECK, M.D., C.M., F.R.C.P.(C.)

Montreal

THIS brief report is a summary of some of our observations with primate growth hormone which are being published in full elsewhere [1, 2, 3]. Our initial observations on the metabolic effects of primate growth hormone in man have been amply confirmed by many investigators [4-16] using growth hormone prepared by a variety of techniques. This presentation concerns the first nine metabolic balance studies carried out with human growth hormone (H.G.H.) in our laboratory, together with observations of its effect on non-esterified fatty acid (N.E.F.A.) metabolism and the possible use of immunochemical methods for the measurement of growth hormone in biological fluids. The growth hormone used for these studies has been prepared by the Raben method [9] and injected intramuscularly in a slightly acid pH.

The blood urea nitrogen and the serum non-protein nitrogen show a significant fall on the second day of H.G.H. administration and this may persist for two to six days after discontinuance of H.G.H. Prompt nitrogen retention occurs, usually apparent on the second day, maximal on the third to sixth day of treatment, and this may persist for three to twelve days after stopping H.G.H. The storage of potassium closely parallels that of nitrogen although equilibrium is achieved more rapidly on cessation of H.G.H. Positive calcium balance is usually achieved by a fall in faecal calcium, although a concomitant increase in urinary calcium occurs. The storage of phosphorus parallels that of calcium and the positive balances may persist after stopping H.G.H., even beyond the time of return to nitrogen equilibrium. A positive sodium balance is frequently observed and in 4 patients this coincided with an increase in urinary aldosterone. This correlation is probably fortuitous since 2 patients showed a marked increase in aldosterone with no significant change in sodium balance. The absence of alteration in urinary 17-ketosteroids and 17-hydroxycorticosteroids during H.G.H. administration suggests minimal or no ACTH con-

tamination in the Raben preparation. Absence of thyroid stimulating hormone (T.S.H.) and antidiuretic hormone (A.D.H.) contamination is supported by the failure to demonstrate any change in  $^{131}\text{I}$  uptake and urine osmolality respectively. A significant fall in urinary ascorbic acid is seen during H.G.H. administration. Alterations in urinary alpha amino nitrogen have only been observed in severe hypopituitary subjects and interpretation of this observation is difficult. No significant change in serum concentration of sodium, potassium, chloride, bicarbonate, calcium, cholesterol, cholesterol esters, total lipids, total fatty acids, lipid phosphorus, mucoproteins and glucosamine has been observed during H.G.H. administration. Total serum inorganic phosphorus showed a tendency to rise during short-term studies but sustained elevations occurred only during prolonged treatment, the latter also being true for the serum alkaline phosphatase (Table I).

TABLE I.—THE EFFECT OF LONG-TERM ADMINISTRATION OF H.G.H. ON THE SERUM INORGANIC PHOSPHORUS AND ALKALINE PHOSPHATASE

D.M.G., aged 16. Panhypopituitarism—H.G.H. Administration

	Feb. 1958	Oct. 1958	Mar. 1959
Serum calcium (mg.%)	10.1		11.0
Serum phosphorus (mg.%)	3.0	5.4	4.4
Serum alkaline phosphatase (K-A units)	8.0	17.4	17.0

Glucose tolerance curve normal October 1958.

Long-term administration of H.G.H. to a 15-year-old pituitary dwarf (Fig. 1) has resulted in an increase in weight of 12 lb. and an increase in height of 1.75 in. (4.4 cm.) over a nine-month period. Although increase in skeletal growth has been demonstrated radiographically, no alteration in bone age has been observed.

H.G.H. in a dose ranging from 200 to 600  $\mu\text{g.}/\text{kg.}/\text{day}$  in hypopituitary subjects has consistently led to impairment of carbohydrate tolerance. This has been manifested by an elevation in the fasting blood sugar, an increase and occasional delay in the peak blood-sugar level and a marked elevation in the two-hour

post-cibal blood-sugar level. These patients have all shown flat glucose tolerance curves after H.G.H. discontinuance. Impairment of carbohydrate tolerance may be seen in the absence of a significant anabolic effect.

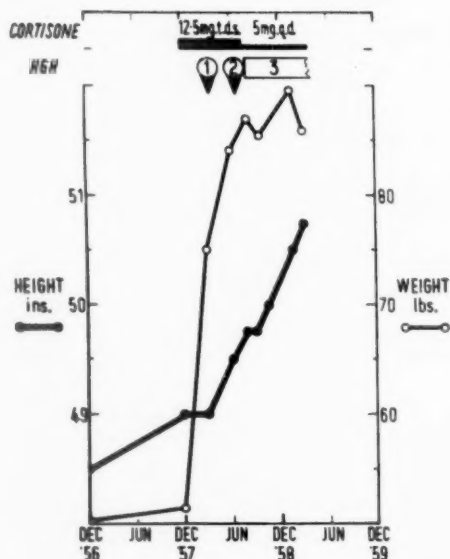


FIG. 1.—Human growth hormone (H.G.H.) administration in a hypopituitary dwarf (D.M., female, born March 1942). The patient received two short courses (1) and (2) of H.G.H. followed subsequently by continuous administration of the hormone (3): (1) H.G.H. 10 mg. per day for four days, 20 mg. per day for two days; (2) H.G.H. 10 mg. per day for fifteen days, tri-iodothyronine 50  $\mu$ g. per day for six days, 25  $\mu$ g. per day for nineteen days; (3) H.G.H. 2.5 mg. three times per week, desiccated thyroid 60 mg. per day from July to October 1958. No thyroid replacement therapy, October 1958 to March 1959.

Evidence for the fat-mobilizing properties of H.G.H. has been obtained by observing its influence on the plasma levels of N.E.F.A. in the fasting human subject. A single intramuscular injection of 5 mg. of H.G.H. produces an initial fall in plasma N.E.F.A. which is maximal after twenty to thirty minutes and is followed by a rise which in the endocrinologically intact individual is maximal between four and six hours. No difference in the N.E.F.A. response has been observed in normals and patients with hypopituitarism using this dose of H.G.H. The N.E.F.A. response appears, in our hands, to be the earliest demonstrable activity produced by H.G.H.

We have been interested in the antigenicity of

various species of growth hormone, of ACTH and of T.S.H. Rabbit antisera to these hormones have been produced and tested by means of a haemagglutination technique in which the antigen is linked to red blood cells by means of bis-diazotized benzidine. Antibodies to bovine, porcine and human growth hormone appear to be species specific. Antibodies to ACTH appear to be hormone specific but not species specific, while the antibodies to T.S.H. show extensive cross-reactions with other pituitary hormones. We believe that immunochemical methods of this type are more sensitive than bio-assay procedures and appear to be useful in the measurement of pituitary hormones in biological fluids.

*Acknowledgments.*—This work was carried out with the close co-operation and practical assistance of Drs. E. E. McGarry, E. H. Venning, I. Dyrenfurth, R. O. Morgen, J. Fishman and E. Bird of the McGill University Clinic, Royal Victoria Hospital, Montreal.

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Meeting

June 24, 1959

**Hyperparathyroidism.**—C. W. H. HAVARD, D.M., M.R.C.P. (for A. W. SPENCE, M.D., F.R.C.P.).

Mrs. W. T., aged 54.

**History.**—1947: Onset of periodic polydipsia and polyuria associated with anorexia, nausea, constipation, headaches and joint pains. Complete remission of symptoms from time to time and equally abrupt relapses. In 1951 the blood pressure was 170/110; blood urea normal; serum calcium 14.8 and 17.8 mg./100 ml.; alkaline phosphatase normal; calcium balance negative; X-rays of skull and cervical spine showed rarefaction. A diagnosis of hyperparathyroidism was made.

In 1952 the neck was explored, but nothing abnormal found. A partial thyroidectomy was performed but no parathyroid tumour was found in the thyroid tissue. After the operation she became severely oliguric. During con-

The diagnosis of primary hyperparathyroidism was confirmed. The surgeons did not consider that a further exploration of the neck or of the mediastinum was indicated at the present time.

1958: Blood pressure 230/130. Blood urea 53 mg./100 ml. Calcium balance showed urinary excretion of calcium to be 270 mg. daily on a 190 mg. calcium diet. Serum amylase 25 Wohlgemuth units. Faecal fat: 11.7 g. excreted daily on a 100 g. fat diet. Stool: no undigested muscle fibres.

January 1959: Blood pressure 210/120. Blood urea 50, serum calcium 12.4, phosphorus 2.3 mg./100 ml.

May 1959: Serum sodium 135, potassium 4.0, chloride 104 mEq./l.; calcium 12.2, phosphorus 3.0 mg./100 ml.; alkali reserve 26.9 mEq./l.; alkaline phosphatase 19 K.-A. units.

**Comment.**—Nephrocalcinosis is now a familiar complication of hyperparathyroidism. More



FIG. 1.—X-ray showing pancreatic calcification in primary hyperparathyroidism.

valence serum calcium readings were 12.6, 14.9 and 11.4 mg./100 ml.

During the years 1953 and 1954 there were no symptoms; blood pressure 190/110; serum calcium 10–11 mg./100 ml. Blood urea 120 mg./100 ml. falling to 50 mg./100 ml. Alkaline phosphatase normal. Alkali reserve normal. 1956: Onset of lower thoracic back pain. 1957: Admitted to St. Bartholomew's Hospital.

**Investigations.**—Serum calcium 12.2, phosphorus 2.4 mg./100 ml. Alkaline phosphatase 10 K.-A. units. Blood urea 32 mg./100 ml. Renal function tests showed impairment of concentration—maximum specific gravity 1018.

**Radiology.**—(1) Extensive calcification in the pancreas (Fig. 1). (2) Osteoporosis of femora and lumbar vertebrae. (3) Tumour of second left rib. (4) Bone cysts in two fingers of right hand. (5) Barium swallow: slight deviation of oesophagus to the right at the level of C.7.

recently pancreatic calcification and recurrent pancreatitis have become recognized as sequelae of this condition and several cases have been reported (Cope *et al.*, 1957; Hoar and Gorlin, 1958). This association is important, for not only may hyperparathyroidism present as pancreatic dysfunction but remission of pancreatitis and indeed some resolution of pancreatic calculi may be expected following removal of the parathyroid adenoma. Pancreatic calcification is almost certainly a more common complication than only 7 published cases might suggest, because a primary hyperparathyroid disorder is not generally considered in patients with pancreatic disease and the abdominal calcification may be misinterpreted as lying within the kidney.

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**Primary Hyperparathyroidism with Four Normal Parathyroid Glands in the Neck and a Mediastinal Parathyroid Adenoma.**—G.

ALAN ROSE, D.M.<sup>1,2</sup> (for D. R. DAVIES, F.R.C.S., and C. E. DENT, M.D., F.R.C.P.).

Mrs. G. W., housewife, aged 44.

**History.**—First admitted to University College Hospital (Metabolic Ward) in February 1957. In 1949, following an attack of acute urinary retention, investigation revealed bilateral renal calculi. She then had right loin pain and a right pyelolithotomy was performed. Shortly afterwards she had left renal colic but then remained reasonably well for some years. 1954: Blood urea 190 mg./100 ml., Hb 67%, blood pressure 130/90. 1955: Admitted with jaundice, anorexia and vomiting; blood pressure 180/110, Hb 48%, blood urea 180 mg./100 ml. Following this she had intermittent urinary infections but was otherwise well until September 1956, when she was tired, losing weight, thirsty and with nocturia, and complaining of bilateral loin pain and low backache. October 1956: Plasma calcium and phosphorus were measured (elsewhere) for the first time and found to be 11.4 and 2.5 mg./100 ml. respectively. She had been a moderate milk drinker until 1954, when she reduced the intake of this on advice. She continued to eat cheese, however, and to drink milk in frequent cups of tea.

**Physical examination.**—Well nourished. Blood pressure 150/110. Fundi showed Grade I changes. Right hypochondrial scar well and normally healed. Tender in both renal angles. No skeletal deformities or tenderness. Crown to pubis 32 in. (81 cm.), pubis to heel 32½ in. (82.5 cm.), span 63 in. (160 cm.). No mass palpable in neck. No corneal calcification.

**Investigations.**—Plasma calcium 12.3, phosphorus 3.3, urea 69 and uric acid 7.0 mg./100 ml. Alkaline phosphatase 10 K.-A. units; albumin 3.5, globulin 2.6 g./100 ml. Plasma ionized calcium 9.45, complexed 0.4 and protein-bound 3.9 mg./100 ml.

Urine sp. gr. maximum 1010, minimum 1005. Twenty-four-hour urine calcium 297 mg. while on a normal calcium diet. Urine contained 0.06% protein, numerous pus cells, but no casts and was sterile. Hb 87%.

Radiology revealed bilateral staghorn calculi with thinning of right renal cortex. No bone changes. Barium swallow normal.

**Course and treatment.**—The diagnosis of primary hyperparathyroidism rested upon the high plasma total and ionized calcium, with hypercalciuria and renal stones for at least eight

years. There was no history of vitamin-D medication or of excess milk or cheese intake while the length of history without onset of overt bone disease excluded rarefying disease of the skeleton.

Mr. D. R. Davies explored her neck on March 6, 1957. He found four parathyroid glands each of which was biopsied and shown to be normal on paraffin section, although the largest one was removed, since frozen section at the time of operation indicated a possible parathyroid adenoma. Post-operatively the plasma calcium rose slightly and at this stage the cortisone test of Dent (1956) was carried out. After ten days of cortisone, 150 mg. a day, the plasma calcium did not fall, indeed it rose very slightly. This excluded vitamin-D overdosage or sensitivity as the cause of the hypercalcaemia. It was concluded that a parathyroid adenoma must still be present, and because the adenoma had not been damaged sufficiently during the operation to cause a temporary fall in plasma calcium it was probably not in the neck (Davies, 1959; Dent, 1959).

On April 3, 1957, Mr. Davies re-explored the neck. During this operation he biopsied the three parathyroid glands previously found, which were shown on frozen section to be normal. He also carried out an extensive search of the neck without finding any more parathyroid tissue. It was then decided, against our usual preference, to split the sternum at this operation as we feared the patient might refuse a third exploration. An obvious chief-cell parathyroid adenoma was found in the anterior mediastinum and on removal weighed 3.3 g.

The patient made a good surgical recovery and the plasma calcium rapidly fell to 5.5 and the phosphorus rose to 5.9 mg./100 ml. These results indicated hypoparathyroidism, as might have been expected since the three remaining parathyroids had each been twice biopsied. She was treated for the hypocalcaemia with dihydro-tachysterol (DHT) in doses up to 2 mg. a day until September 1, 1958 (see Fig. 1). In November 1957 an attempt was made to stop the DHT, but the plasma calcium quickly fell to 6.4 mg./100 ml. and she developed paraesthesiae. It was necessary to continue the DHT until September 1958, since when she has been symptom-free without treatment, and the plasma total calcium values have not been lower than 7.9 mg./100 ml. It is presumed that in the two years since operation the parathyroid glands have regenerated sufficiently to maintain the plasma calcium at an adequate level, and that this level will slowly rise to normal.

The blood urea rose in the immediate post-operative period but rapidly fell again, and for

<sup>1</sup>In receipt of a grant from the Medical Research Council.

<sup>2</sup>Medical Unit, University College Hospital, London.

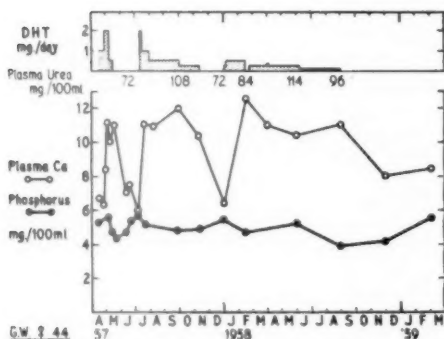


Fig. 1.—Plasma calcium and phosphorus levels after removal of parathyroid adenoma. Withdrawal of dihydrotachysterol was followed by return of tetany in November 1957, but not in September 1958.

the last two years has remained between 72 and 108 mg./100 ml. The blood pressure continues to be elevated at about 155/115 on outpatient readings. Urine calcium is now very low.

As far as we know this is the first recorded instance in which it has not been possible to exclude primary hyperparathyroidism after finding four normal parathyroid glands. Of interest, too, is the slow recovery during seventeen months of the small residuum of normal parathyroid tissue.

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#### Hirsutism Associated with a Testosterone-producing Ovarian Cyst.—IVOR H. MILLS, Ph.D., M.D., M.R.C.P., and R. V. BROOKS, Ph.D. (for F. T. G. PRUNTY, M.D., F.R.C.P.).

A woman aged 25 complained of vaginal bleeding for six months and of having felt an abdominal mass for three months. One year previously she had been delivered of a premature infant at 36 weeks of pregnancy. Delivery was normal and she breast fed the baby for one month. Six months later intermenstrual bleeding was noticed and hair began growing on her face, which by the time she came to hospital had to be shaved daily. There had been no change in her voice. The hirsutism involved her face, legs and abdomen. There was a large soft mass arising out of the pelvis, displacing the uterus to the right. The clitoris was definitely enlarged. Physical examination was otherwise normal. The blood picture, plasma electrolytes and glucose tolerance test were normal. The resting 17-ketosteroids were 11.3 and 8.4 mg. per day and on the fourth day of 20 units of ACTH gel b.d. intramuscularly rose to 14.2 mg. Ketogenic steroids were 5.8 and 8.2 mg. per day

and rose after ACTH to 38.6 mg. Fractionation of the 17-ketosteroids showed a normal pattern except that the ratio of androsterone plus etiocholanolone to the two 11-hydroxy derivatives of these compounds was above that found in 6 normal people. Urinary oestrogen excretion (Drs. R. D. Bulbrook and F. C. Greenwood) was oestrone 5.0, oestradiol 3.2, oestriol 5.3 µg./day (within normal range). At operation (Mr. A. J. Wrigley) a large multilocular ovarian cyst (25 × 45 × 30 cm.) was removed. This contained numerous large cysts filled with thin yellowish fluid. Histological examination of the tumour showed the cysts were separated by fibrous septa and lined with several layers of cuboidal epithelium (Fig. 1) having the appear-

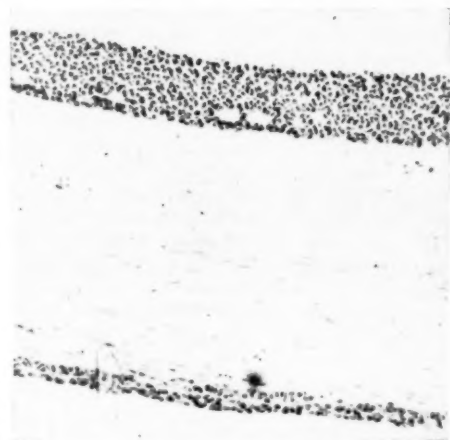


Fig. 1.—Section of septum between loculi of tumour. Typical Call-Exner bodies are present in upper layer of cuboidal cells.

ance of granulosa cells. Call-Exner bodies were present in this epithelium. The tumour therefore appeared to be of follicular origin. The endometrium was postmenstrual in type.

10 grams of the epithelial strippings of the tumour were incubated at 37° C. for three hours in Krebs-Ringer bicarbonate buffer with the addition of nicotinamide, DPN, fumaric acid and ATP and in the presence of 500 mµc <sup>14</sup>C-4-progesterone. The buffer was extracted and the following non-radioactive steroids added: androstenedione 92 µg., testosterone 80 µg., 17-hydroxy-progesterone 100 µg., and progesterone 80 µg. By successive chromatography combined with acetylation, chromic oxidation and alkaline hydrolysis, it was found that 43% of the radioactive progesterone remained unchanged, 4.6% was converted to 17-hydroxy-

progesterone and 0.6% to testosterone. The production of androstenedione was not definitely established.

The formation of testosterone by ovarian tissue has previously been shown by Savard *et al.* (1957) and by O'Donnell and McCaig (1959). Despite the small amount of testosterone formed *in vitro* (of the same order as found by other workers) it is probable that because of the enormous size of the tumour sufficient testosterone was being produced to account for the virilism in this patient. This type of tumour is usually associated with oestrogen production and it is somewhat surprising that oestrogen excretion was normal. However, the pathway to oestrogen has been shown to pass through androgen (Wotiz *et al.*, 1956; Baggett *et al.*, 1956) and to be stimulated by F.S.H. (Hollander and Hollander, 1958). In this case the biosynthesis of oestrogen may have been partially arrested at the androgen stage. That androgen was being produced in excess might also be deduced from the poor 17-ketosteroid response to ACTH. It is possible that the second pituitary hormone which is synergistic with ACTH in the control of adrenal androgen (Prunty, 1956) might have been partially suppressed by androgens of ovarian origin. An extra-adrenal source of androgen is also suggested by the high ratio of androsterone plus etiocholanolone to the two 11-hydroxy derivatives of these compounds since the latter are produced only in the adrenal whereas the former would also arise from the ovarian testosterone.

The data are in conformity with the view that the virilization of this patient resulted from testosterone production in the large follicular ovarian cyst.

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**Adrenal Virilism.**—C. W. H. HAVARD, D.M., M.R.C.P. (for A. W. SPENCE, M.D., F.R.C.P.).

Miss E. S., aged 33.

**History.**—1937: Menarche aged 11. 1940: At the age of 14 began to grow hair on the beard area. Periods became increasingly scanty and irregular. 1947: Admitted under the care of Dr. E. F. Scowen for investigation of hirsuties

of face, limbs, chest and abdomen. External genitalia normal. Urinary 17-ketosteroids (26.3.47) 13 mg./24 hours. Glucose tolerance test: fasting blood sugar 157 mg., half hour 298 mg., one hour 282 mg., one and a half hours 257 mg., two hours 189 mg./100 ml.

April 1947: Removal of left adrenal gland, found at laparotomy to be larger than the right. Histological examination revealed no abnormality. Post-operatively the glucose tolerance test was normal. The operation was followed by an excellent response: the beard thinned and later disappeared and the skin became less coarse and pustular. Urinary 17-ketosteroids/twenty-four hours: 14.5.47, 8.4 mg.; 23.5.47., 9 mg.



A



B

FIG. 1.—Facial hirsuties in adrenal virilism. A, before treatment; B, after treatment with oral prednisolone.

1957: Recurrence of hirsuties. Less energy; hot flushes affecting the head and neck appeared. Periods became very heavy.

*On admission* (April 1958).—Marked hirsuties affecting the beard area, limbs, chest and abdomen; male distribution of pubic hair. No striae. Slight hypertrophy of clitoris. Blood pressure 120/80. No glycosuria.

*Investigations.*—Glucose tolerance test: fasting blood sugar 140 mg., half hour 164 mg., one hour 130 mg., one and a half hours 127 mg., two hours 106 mg./100 ml.

Urinary 17-ketosteroids/twenty-four hours: 11.4.58, 14.1 mg.; 19.4.58, 18.0 mg.; 23.4.58, 11.9 mg.; 25.4.58, 15.4 mg.

Urinary 17-hydroxycorticoids/twenty-four hours: 19.4.58, 17.5 mg.; 23.4.58, 9.0 mg.; 25.4.58, 16.5 mg.

*Treatment and progress.*—Oral prednisolone 30 mg. daily for one week suppressed adrenal activity and the urinary 17-ketosteroids fell to 2.6 mg./twenty-four hours. Steroid therapy was then slowly reduced to a maintenance dose of 5 mg. twice daily. A dramatic response followed. Ten days after beginning treatment the facial hair literally fell out and a few weeks later much of the excessive hair on the limbs disappeared; the pubic hair remained unchanged. No recurrence of hirsuties has occurred on maintenance steroid therapy.

*Comment.*—The disappearance of hirsuties in this patient as a result of steroid therapy is exceptional because usually the response is disappointing (Spence *et al.*, 1956; de Mowbray *et al.*, 1959).

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#### Acromegaly Occurring in One of Uniovular Twins.

—J. H. BRIGGS, M.R.C.P. (for P. M. F. BISHOP, D.M., F.R.C.P.).

D.B., male aged 24.

*Presenting symptom.*—Swelling of right breast for three years. On direct questioning he admitted to sweating attacks. There had been a weight gain of about 1 st. in the last two years. Weight 11 st. 10 lb., height 5 ft. 11 in.

*On examination.*—Well-marked gynæcomastia on right side which was tender, the left being normal. Some heaviness of the features and an abnormal occlusion of the incisors which he thought was due to an injury to the tooth. No glucosuria.

*Investigations.*—E.S.R. 9 mm. in first hour (Westergren), B.M.R. +2%, serum calcium



FIG. 1.—Monozygotic twins aged 24. The patient (left of picture) has early soft-tissue and bony changes affecting the face, large and most numerous fleshy warts, and right gynæcomastia.

10.5, phosphorus 4.6 mg./100 ml., alkaline phosphatase 6.4 K.-A. units. Comparison of glucose tolerance and glucose-insulin tolerance tests showed insulin resistance. Blood pyruvates were normal. Forty-eight-hour protein-bound <sup>131</sup>I less than 0.04%, T index 2.7, twenty-four-hour urinary gonadotrophins 6–24 mouse units, 17-ketosteroids 12.3 mg./twenty-four hours. Body composition studies using bromine 82 and tritium were carried out in both the patient and his twin brother before and after the treatment and showed no significant change. Blood groups are identical and favour a monozygotic relationship 8:1. X-ray of skull showed that the sella is enlarged in its anteroposterior diameter and the dorsum is thinned; the posterior clinoid processes appeared eroded from below.

*Progress.*—He was treated with radiotherapy 3,500 r from a 250 kV source given over three weeks, after which he felt better and sweated less.

The glucose tolerance and glucose-insulin tolerance tests reverted to normal. The alteration in weight in the twelve months following treatment was less than 2 lb.

Right mastectomy was performed for cosmetic

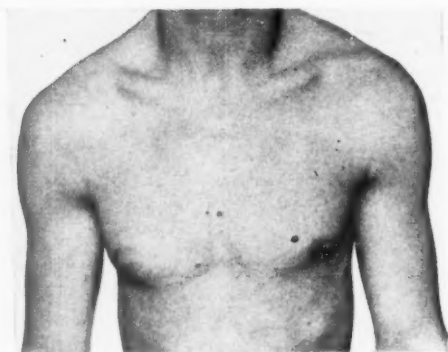


FIG. 2.—Patient with right gynecomastia.

reasons in February 1958: histological examination showed dense collagenous fibrosis.

The twin brother, Alan, was interviewed and examined. He is normal (weight 10 st. 8 lb., height 5 ft. 10 in.). He said that up to the age of 20 years friends had difficulty in identifying them but that this was no longer so.

*Comment.*—As far as we are aware, there is one other authentic example of acromegaly occurring in one of uniovular twins, reported by Lewis (1934). In this patient the disease commenced earlier and resulted in a difference in height of 8½ in. and in weight of almost 6 st.

*Acknowledgment.*—We wish to thank Dr. J. Gibbons of the Maudsley Hospital for assistance with tritium counting.

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**Pituitary Tumour Following Adrenalectomy for Cushing's Syndrome.**—K. F. R. SCHILLER, B.M., M.R.C.P. (for A. STUART MASON, M.D., M.R.C.P.). Mrs. D. R., aged 27.

*First Admission* (November 1956)

Previously healthy English woman of normal colouring and appearance (Fig. 1A), admitted with eight months' history of progressive weight increase, rounding of face, deposition of fat over nape of neck and abdomen, increasing hirsuties of limbs and face with facial acne, and menstrual irregularity. No headaches or visual symptoms.

*On examination.*—Facial appearance (Fig. 1B) and bodily habitus typical of Cushing's syndrome. Blood pressure 145/105.

*Investigations.*—Serum electrolytes normal. Urinary 17-ketosteroids 37 mg./day. Glucose tolerance test: fasting level 87 mg./100 ml.,

two-hour level 154 mg./100 ml. X-ray pituitary fossa normal (Fig. 2A).

*Operation* 12.12.56 (Mr. J. E. Richardson).—Bilateral adrenal hyperplasia: total right (9.5 grams) and 9/10 subtotal left (7.5 grams) adrenalectomy. Good response to operation, with loss of stigmata of Cushing's syndrome.

*Progress.*—Discharged on cortisone 12.5 mg. daily, this being progressively reduced. Developed symptoms suggestive of hypo-adrenalism, became steadily more pigmented and readmitted for stabilization.

*Second Admission* (April 1957)

Generalized deep cutaneous pigmentation especially over creases, nipples and scars, with pigmented patches on oral mucosa. Very languid. Blood pressure 90/70.

*Investigations.*—Serum electrolytes: Sodium 137, chloride 97, potassium 5.1 mEq./l.

*Progress.*—Satisfactory stabilization achieved with cortisone 37.5 mg. and fludrocortisone 0.1 mg. daily without salt supplements. X-ray of pituitary fossa December 1957 normal (Fig. 2B). Pigmentation deepened progressively and very considerably until:

*Third Admission* (December 1958)

Five months' migraine-like headaches radiating to right upper canine; four months' increasing tendency to diplopia and progressive failure of vision of left eye.

*On examination.*—Skin deeply pigmented with pigmented oral patches. No residual characteristics of Cushing's syndrome. Right ptosis; right eye slightly proptosed with circumorbital oedema (Fig. 1C); right pupil dilated and fixed; right external ocular movements limited to few degrees outward and downward movement. Visual acuity: right 6/9, left 6/60. Fundi: right myopic peripapillary atrophy; left macular chorioretinal haemorrhage; no papilloedema on either side. Visual fields: small right upper temporal defect; large left centrocaecal scotoma breaking through to temporal quadrants. Blood pressure 120/90.

*Investigations.*—Serum electrolytes: normal. Serum cholesterol 260 mg./100 ml. Radioiodine test: twenty-four-hour neck uptake = 26%; urinary excretion: twenty-four to forty-eight hours = 4%. X-ray pituitary fossa (Fig. 2C) showed backward displacement and erosion of both posterior clinoid processes and marked increase in size of fossa since December 1957 (Fig. 2B).

*Treatment.*—Telecobalt 60 irradiation to pituitary from both temples (Dr. Walter Shanks), total dose 4,500 rads.



FIG. 1A.



FIG. 1B.



FIG. 1C.



FIG. 1D.

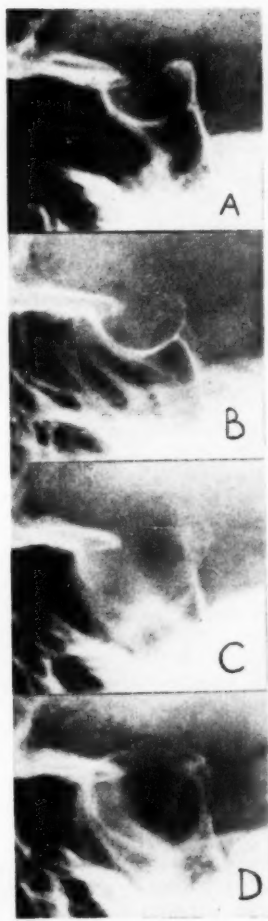


FIG. 2.

#### *Progress since Third Admission to June 1959*

The headaches disappeared and the eye signs improved rapidly, but residual limitation of movement of the right eye, enlargement of fixed right pupil, diminution of left visual acuity and left temporal field defect persist. Pigmentation is less (Fig. 1D) and the blood pressure 100/70 on treatment as above. There has been no return of catamenia since May 1958. There is certainly no change suggestive of a return of Cushing's syndrome, but the skin is coarser, the face filling out and there is an increase in weight. The clinical impression of myxedema was confirmed.

*Investigations.*—Serum cholesterol 355 mg./100 ml. Radioiodine test: twenty-four-hour

neck uptake 30%. Plasma protein-bound iodine 1.5  $\mu\text{g.}/100$  ml. X-ray pituitary fossa (Fig. 2D) shows no decrease in size but evidence of recent recalcification.

*Discussion.*—Following the cure of Cushing's syndrome by adrenalectomy this patient developed progressive deep pigmentation of Addisonian type despite the correction of hypo-adrenalism with steroid therapy. She subsequently presented clinical and radiological signs of a rapidly growing pituitary tumour. Excess of a substance having the properties of melanophore stimulating hormone (M.S.H.) was found in her serum and urine. Irradiation of the tumour reduced its size, pigmentation became less marked and M.S.H. levels fell (Mitchell, 1959).

Similar cases have been described by Nelson *et al.* (1958) and Rees and Bayliss (1959). In all 3 cases the pituitary tumour was associated with gross pigmentation which faded when the tumour was irradiated or removed. There seems no doubt that these tumours produce M.S.H.: raised levels were found in all 3 cases. As the output of this hormone closely parallels ACTH production (Sulman, 1956) it is reasonable to surmise that these tumours also produce excess ACTH: high levels of serum ACTH were found in the cases of Nelson *et al.* (1958) and Rees and Bayliss (1959).

In our patient we suggest that the initial Cushing's syndrome associated with adrenal hyperplasia was due to pituitary over-activity with an alteration in sensitivity rather than an abolition of the pituitary-adrenal feed-back mechanism after adrenalectomy. Thus there developed an unusual degree of pituitary autonomy: in the case of Nelson *et al.* (1958) this was the suggested explanation when intravenous hydrocortisone did not suppress ACTH production. Such autonomy has also been achieved experimentally in animals (Furth, 1955). We suggest that in our case adrenalectomy altered the inhibitory effect of adrenal steroids on the pituitary, and allowed a more rapid growth of pituitary tissue. Edmunds *et al.* (1958) invoke the antagonistic actions of cortisone and aldosterone on the pituitary to explain the disappearance of pigmentation in a case of adrenal hyperplasia following adrenalectomy.

We have also observed a patient who became deeply pigmented after adrenalectomy for Cushing's syndrome but for two years has shown no evidence of developing a pituitary tumour. Spence (1957) quotes a similar case; Sprague (1953) mentions several instances while reviewing a post-operative series of 50 cases of Cushing's syndrome.

Deep pigmentation following adrenalectomy for Cushing's syndrome suggests that a pituitary tumour is forming: the histological nature of such tumours is variable and the prognosis uncertain.

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#### Hypertension and Hypokalaemia Associated with Hypo-aldosteronism.—E. J. Ross, M.D.

T. B., schoolboy, aged 13 years.

*History.*—Symptomless hypertension found at a school medical examination. Paternal grandmother was hypertensive. No history of renal disease.

*Physical examination.*—Short stature. Left ventricular enlargement. Apical grade 2 systolic murmur. Blood pressure 200/140. Grade 2 hypertensive retinopathy.

*Relevant investigations.*—Plasma electrolytes: Sodium 144–148, potassium 2.7–3.0, carbon dioxide 30–34, chlorides 96–100, magnesium 1.39 mEq./l. Arterial pH 7.45. Urine pH 6–9. Muscle biopsy showed decreased potassium and increased sodium content. Amphenone reverted biochemical abnormalities towards normal.

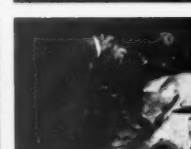
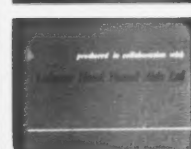
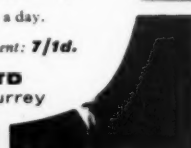
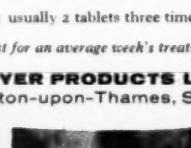
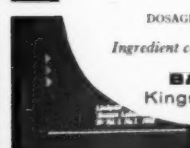
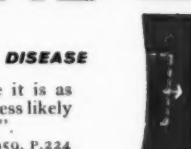
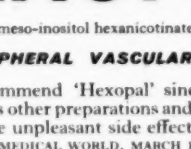
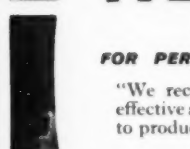
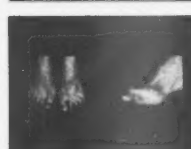
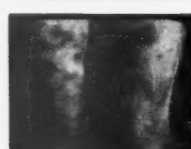
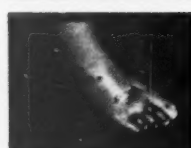
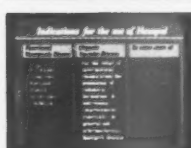
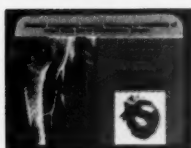
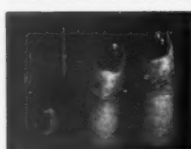
*Investigation of steroid metabolism.*—Normal 17-ketosteroids and 17-ketogenic steroids. Aldosterone excretion 0.3 µg./day. Tetrahydroaldosterone absent. Aldosterone secretion rate (using tritiated aldosterone); 4 µg./twenty-four hours. Paper and column chromatography showed presence of abnormal steroid pattern.

*Operation.*—Adrenal exploration. Both adrenals were small. No evidence of tumour. Bilateral adrenalectomy performed. Hypertension, abnormal steroid excretion and abnormal plasma electrolyte concentrations persisted after removal of both adrenals. Patient developed signs of adrenal insufficiency eight days after withdrawal of cortisone maintenance therapy.

*Comment.*—The patient presented with hypertension and the biochemical abnormalities characteristic of Conn's syndrome. However, urinary aldosterone excretion and aldosterone secretion rates were both too low to be measured with accuracy. Despite the virtual absence of aldosterone, adaptation to a low sodium diet was normal, but adaptation to a low potassium diet poor. The similarity to Conn's syndrome suggested the excretion of excessive amounts of a sodium-retaining hormone, but none was detected by bio-assay. Bilateral adrenalectomy was ineffective, and suggests the presence of an undetected tumour. This case is thought to be an abnormality of adrenocortical biosynthesis resulting in a syndrome resembling that described by Conn (1955). Full details of the biochemical findings will be published elsewhere.

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## *Section of Experimental Medicine and Therapeutics*

President—M. L. ROSENHEIM, C.B.E., F.R.C.P.

Meeting  
May 12, 1959

### **Pharmacology of Cardiac Failure**

By J. H. BURN, M.D., F.R.S.

*Oxford*

CARDIAC failure calls to mind first of all a decline of the circulation which is a consequence of progressive weakness of cardiac muscle, and the pharmacology of cardiac failure suggests a reappraisal of the action of digitalis. The form of failure which is, however, characteristic of cardiac muscle is ventricular fibrillation, and it is the pharmacological aspects of fibrillation which we have studied at Oxford during the last four and a half years. I suppose it is true that in most cases fibrillation of the ventricles is the prelude to cardiac failure.

It will be simplest to begin at the end and to explain the hypothesis at which we have arrived and then to consider the evidence in favour of it. This is the reverse of the logical order, but it is then easier to see how far the evidence supports the view. For this purpose let us consider the changes in electrical potential which occur in an atrial or ventricular fibre during the course of contraction. There is an electrical potential across the fibre membrane, the inside being negative relative to the outside, and during diastole the difference is about 85 millivolts. This difference is sometimes called the transmembrane potential. Immediately before contraction begins the negative charge inside the fibre disappears and is indeed reversed to one which is positive. The removal of the internal negative charge, which is a depolarization, is the first step of what is called the action potential. The first step is the same in other tissues such as skeletal muscle and nerve. But thereafter the action potential in cardiac muscle is different. Whereas in skeletal muscle and in nerve there is a prompt restoration of the charge on the membrane so that it is quickly repolarized in a few milliseconds, in cardiac muscle there is a long delay during which the state of depolarization persists. Only after a period as long as 150 to 200 msec. does repolarization occur. Now during this long period in which the cardiac muscle fibres are depolarized they are inexcitable. The plateau in the cardiac action potential is therefore a period of inexcitability.

Thus cardiac muscle differs from other tissues in which electrical impulses are propagated, in having a long period after each impulse during which a second impulse is ineffective. It seems not unreasonable to suggest that the long refractory period exists for a purpose, and that the plateau in the action potential is a device to ensure that one group of fibres is not excited by activity in an adjacent group, and thus to make certain that the fibres of cardiac muscle contract only in response to impulses arriving from the pacemaker.

In atrial muscle impulses leave the pacemaker at a rate which is normally about 70 per minute, but may rise to twice this or more. These impulses find their way to the different parts of the atria along different pathways. We ordinarily assume that the rate of conduction at any one point of time is constant throughout the atria, and that impulses reaching adjacent, or nearly adjacent, fibres arrive at the same moment. However, when we reflect on what we know of biological properties such as rate of conduction, we remember that the experience of the last thirty years has shown that they are never constant, but show a surprising degree of variation. Hitherto there have been no observations on the rates of conduction from the pacemaker to different but adjacent points on the atria. When impulses are sent out at ordinary rates and when metabolic processes are producing normal amounts of energy, it may well be that the difference in rates of conduction to adjacent points is small. When, however, stimuli are sent out at a high rate, as from an ectopic focus, and when metabolic processes are less effective, it may then happen that the rates of conduction differ, and that an impulse may reach one point A before it reaches an adjacent point B. Now if the fibre at the point A were to be quickly repolarized and made re-excitable, it might then be excited for a second time by the spread of excitation from the fibre at point B. In this way a local extrasystole would occur. Normally re-excitation of one fibre by another is prevented

by the plateau in the action potential which maintains a state of inexcitability. But whenever the plateau is diminished and the action potential is appreciably shortened extrasystoles, flutter, and finally fibrillation seem to occur.

Let us now consider the evidence for this view.

*Atrial fibrillation and acetylcholine.*—In 1955 my colleagues Vaughan Williams and Walker and I discovered that we could produce atrial fibrillation at will and maintain it for as long as we wished (Burn *et al.*, 1955). We worked with the Starling heart-lung preparation of the dog, and applied electrodes to the tip of the right atrium. A short burst of stimuli, say at the rate of 800 per minute, applied for 2 minutes, disturbed the rhythm while stimulation was applied, but the normal slow rhythm returned as soon as the stimulation was cut off. If, however, we infused acetylcholine at a constant rate into the superior vena cava, and re-applied the same short burst of stimuli, we produced atrial fibrillation which persisted for so long as the infusion of acetylcholine was maintained, whether this was five minutes or one and a half hours. When the infusion was stopped a normal rhythm returned.

It has of course been known for a long time that vagal stimulation (Andrus and Carter, 1930) and acetylcholine favoured atrial fibrillation. Nahum and Hoff (1940) produced fibrillation by applying acetyl- $\beta$ -methylcholine to localized regions on the atrial surface. Scherf *et al.* (1948) produced fibrillation by application of aconitine, but this method also involves acetylcholine, being, for example, always abolished by atropine. Our method, however, was the first in which fibrillation could be maintained as long as desired and terminated at will.

*Ventricular fibrillation.*—In 1957 Armitage and Gunning and I studied ventricular fibrillation in the isolated rabbit heart (Armitage *et al.*, 1957). Again we applied a high rate of electrical stimulation, this time direct to the ventricles, and determined the duration of the disturbance of the rhythm after stimulation had stopped. We found that carbachol and atropine had no effect on the duration of the disturbance and therefore concluded that acetylcholine, which resembles carbachol in its action, played no part in facilitating ventricular fibrillation, and that its relation to the ventricles in this respect was quite different from its effect on the atria.

In 1953 Hoffman and Suckling studied the effect of acetylcholine on the action potential of atrial fibres and of ventricular fibres in the dog heart. They observed that in the atria acetylcholine had a great effect in reducing the duration of the action potential but that in the ventricles it had no effect whatever. The reduc-

tion in the duration of the atrial action potential was from a normal value of 150 msec. or more to one of 10 msec., that is to about one-fifteenth of the normal value. These observations suggested the hypothesis that the effect of acetylcholine in facilitating atrial fibrillation was due to its action in shortening the duration of the action potential and so causing rapid restoration of excitability in atrial muscle; its failure to facilitate ventricular fibrillation was explained by the lack of any effect on the duration of the ventricular action potential.

I have therefore made the suggestion that in the circumstances in which we have produced it experimentally, fibrillation is not due to a circus movement in the first place, or to a high rate of discharge from an ectopic focus in the second place, but to a shortening of the action potential to such a point that when adjacent fibres are out of phase, as after receiving a burst of rapid stimuli, they are then able to stimulate one another. This stimulation of one fibre by an adjacent fibre will continue throughout the mass of atrial fibres so long as the atrial action potential remains of short duration, that is to say so long as acetylcholine is infused. When the infusion is stopped the action potential lengthens and excitation of any fibre by an adjacent fibre ends. The pacemaker takes over and a normal rhythm is resumed.

*Factors which shorten the action potential.*—We must now consider whether other factors, known to shorten the duration of the action potential, also facilitate fibrillation. There is evidence that the maintenance of the plateau, and so of an action potential of long duration, is a process which requires energy, and that when energy is lacking the plateau diminishes in length. The evidence has been provided by a study of the effect of metabolic inhibitors. One method of diminishing available energy is to add dinitrophenol to the solution surrounding the heart. Part of the energy made available by oxidation is normally used for the purpose of phosphorylation, to convert adenosine monophosphate and adenosine diphosphate into adenosine triphosphate. In the presence of dinitrophenol the energy from oxidation cannot be used in this way. Macfarlane and Meares (1955) have shown that dinitrophenol reduces the plateau of depolarization in the atrium and ventricle of the frog to about one-third of its normal length, and Kuschinsky *et al.* (1958) have shown that it reduces the duration of the action potential in the atrial muscle of the rat. Provided the concentration was not too high Macfarlane and Meares found that the effect was reversible. In keeping with this observation we found that the addition of dinitrophenol to the fluid perfusing

the rabbit heart caused persistent fibrillation to follow electrical stimulation of the ventricles. The method used was to set up an isolated rabbit heart and to stimulate the ventricles at a high rate in conditions in which a normal rhythm promptly returned when the stimulation stopped. We then added dinitrophenol to the perfusing fluid and repeated the stimulation. We found that stimulation then caused fibrillation which persisted when the stimulation stopped. This effect of dinitrophenol was reversed when it was removed from the solution (Armitage *et al.*, 1957).

Macfarlane (1956) found that sodium azide also reduced the duration of the action potential of the frog, and in keeping with this Goodford (1958) found that in the presence of sodium azide rapid stimulation of the ventricles led to persistent fibrillation just as in the presence of dinitrophenol.

Another active substance which is also a metabolic inhibitor is sodium monoiodoacetate. Lüllmann (1959) found it shortened the duration of the action potential in the atria of the rat, and Goodford (1958) observed that when it was added to the fluid perfusing the heart, rapid stimulation of the ventricles caused persistent fibrillation. This effect, however, unlike that of dinitrophenol and azide, was not reversible.

*Action of adrenaline in atrial fibrillation.*—The action of adrenaline on the atria is the direct opposite of acetylcholine. Webb and Hollander (1956a) studied its effect on the atrial action potential, and found that adrenaline prolonged the action potential in the atria of the rat. In keeping with this we found that when adrenaline was infused at constant rate into the heart-lung preparation at the same time as acetylcholine was infused, electrical stimulation of the atria no longer caused atrial fibrillation. Adrenaline counteracted the fibrillatory action of acetylcholine.

*Variations in calcium ion concentration.*—We have made several studies of the effect of altering the concentration of  $\text{Ca}^{++}$  on fibrillation, and the latest by Milton (1959) has shown that at 32° C. the proportion of hearts in which stimulation caused persistent fibrillation was in linear relation to the  $\text{Ca}^{++}$  concentration, increasing as the concentration rose. Now as long ago as 1936 Schütz stated that in high-calcium solutions cardiac muscle becomes re-excitabile at a relatively early stage of repolarization. Hoffman and Suckling (1956) have since found that in papillary muscle when the amount of calcium was high repolarization occurred at a faster rate, while when the amount of calcium was low the action potential was longer, due to a prolongation of the plateau.

Thus we have a series of factors, the metabolic inhibitors dinitrophenol, sodium azide and monoiodoacetate, adrenaline (acting on the atria) and calcium ion concentration, all of which either shorten the duration of the action potential and increase fibrillation, or lengthen the action potential and decrease fibrillation.

*Oxygen lack.*—The evidence concerning the effect of oxygen lack on action potential also supports our hypothesis but the relationship is not so straightforward. Trautwein *et al.* (1954) and also Webb and Hollander (1956b) showed that oxygen lack shortened the duration of the action potential, and it may be deduced from our observations that oxygen lack facilitates fibrillation. We found that a fibrillating heart always returned to a normal rhythm when ice-cold saline was poured over the outside, confirming Dirken *et al.* (1955), and we were for a long time unable to understand this. The effect of temperature was studied by Beaulnes and Day (1957) in the isolated atria, and they found that when fibrillation was induced at 37° C. it could be terminated by cooling to 32° and then re-established by raising the temperature to 37° again. Goodford (1958) made identical observations in the ventricles.

Since in cardiac surgery the occurrence of fibrillation is a greater danger when the temperature is low these results were unexpected. The explanation of them, however, may be as follows. When an isolated heart is perfused at 37° C. with a modification of Locke's solution the heart depends for its oxygen supply on what is carried in solution, which is of course much less than that present in the blood. The heart may therefore be on the border of anoxia. If anoxia facilitates fibrillation, we would have an explanation of the occurrence of fibrillation in about 40% of normal hearts following electrical stimulation at 37° (Armitage *et al.*, 1957; Kärki, 1958). If, however, the temperature is dropped to 32° C. the demand of the heart for oxygen falls, and, the supply of oxygen remaining the same, the heart moves farther away from anoxia. It is in fact difficult to provoke fibrillation by electrical stimulation at 32° except in an occasional heart (Milton, 1959).

Support for the view that anoxia facilitates fibrillation was given by Goodford's experiments with cyanide. In a series of experiments he observed that the addition of cyanide to the perfusing fluid resulted in stimulation causing persistent fibrillation. This evidence was, however, complicated by other evidence showing that either cyanide or total deprivation of oxygen would cause hearts which were already fibrillating to revert to normal rhythm. The situation is therefore not simple though further work should clarify it.

**Potassium concentration.**—The effect of stimulation in atria and in the ventricles also depends upon the concentration of  $K^+$ . As the  $K^+$  concentration was reduced the proportion of hearts increased in which stimulation caused fibrillation. Atrial fibrillation, induced in the heart-lung preparation, was arrested when KCl was slowly infused into the blood so as to raise the  $K^+$  concentration from 5 to 8 mEq./l. Recently Lüllmann (1959) has found that a rise in  $K^+$  concentration from 2.7 to 8.1 mEq./l. increased the duration of the action potential in the atria of the rat and of the cat, so that the effect of changes in  $K^+$  also fits with the hypothesis.

**The action of quinidine.**—A study of the action of quinidine on the atrial action potential by Vaughan Williams (1958) has shown that it decreases the rate of rise of the upstroke of the action potential and as a consequence increases the effective refractory period. No observations have yet been made, however, on the effect of quinidine when the action potential is first made short by the presence of acetylcholine. Since in all tissues quinidine appears to antagonize the action of acetylcholine, it may well prolong the shortened action potential.

**Cause of fibrillation.**—The clue to the occurrence of fibrillation may lie in the need of the heart for energy for two quite different purposes. In appropriate conditions an isolated heart maintaining a normal rhythm at 32°C. passes into fibrillation when the temperature is raised to 37°. This event seems to be a precise parallel to the occurrence of fibrillation on raising the temperature from a low point when cardiac surgery has been completed. The fibrillation may occur because the energy available as the temperature rises is not sufficient to satisfy the requirements of both the contractile mechanism and of the mechanism for maintaining an action potential of sufficient duration.

Similar ideas are applicable to the action of adrenaline on the ventricles. When the isolated heart is stimulated electrically at a high rate in conditions in which a normal rhythm returns when the stimulation ends, the addition of adrenaline to the perfusing solution changes the situation. A further period of stimulation then causes fibrillation. It may be that adrenaline by increasing the rate and force of the contractions increases the oxygen usage, so that much less oxygen is available for the maintenance of an action potential of long duration. Adrenaline may act in a similar way when it causes fibrillation in a dog under chloroform anaesthesia, for under chloroform the processes supplying energy are probably diminished.

**The action of adenosine triphosphate.**—As a means of reducing the risk of fibrillation, the

use of adenosine triphosphate should be considered, for we found that in the ventricles of the isolated heart adenosine triphosphate was effective in arresting fibrillation. It was possible to arrest and to re-establish ventricular fibrillation several times by first adding and then withdrawing adenosine triphosphate from the perfusion fluid. We tested adenosine monophosphate and also inosine triphosphate to see if they had the same action and found that they had not. In several other experiments in the heart-lung preparation which have not been published, Gunning, Walker and I found that adenosine triphosphate was also able to arrest atrial fibrillation, especially in the presence of magnesium. We are unable to explain this action of adenosine triphosphate, which is not likely to be exerted within the cell since it is thought not to penetrate the cell. It is, however, a point of the greatest interest that the maintenance of the plateau of the action potential, which prevents fibrillation, appears to be linked to supplies of high energy phosphate such as adenosine triphosphate. Whatever its mode of action, adenosine triphosphate may be worth trying clinically to prevent fibrillation in circumstances when the risk of fibrillation is great. It might perhaps be administered as an intravenous drip without exposing the patient to any foreseeable danger.

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## Section of Psychiatry

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Meeting  
June 19, 1959

MEETING AT GRAYLINGWELL HOSPITAL, CHICHESTER

### Observations on the Chichester and District Mental Health Service

By JOHN MORRISSEY, M.D., D.P.M., and PETER SAINSBURY, M.D., D.P.M.

Chichester

THE Chichester and District Psychiatric Service was started on January 1, 1958. It serves the Western half of the County of West Sussex, which has a mainly rural population of approximately 112,000. The only large towns in the area are Chichester and Bognor, with a combined population of some 44,000. The Out-Patient Department is at the Royal West Sussex Hospital in Chichester and the Day Hospital is at Summersdale. The organization of domiciliary and day hospital treatment follows closely that of the original scheme in Worthing. The medical staff consists of three Psychiatrists, Dr. Morrissey, Dr. J. Towers and Dr. J. P. Scrivener, and two Registrars.

The aim of this service was to find out whether similar results to those obtained during the previous year in Worthing (Carse *et al.*, 1958) could be achieved (a) by other workers, (b) in a more scattered and more rural area, and (c) by medical staff who had to spend at least half their time on in-patient work.

During the year 842 new patients were seen. This gives a referral rate for the administrative areas of West Sussex served of 7.5 per 1,000 population. The referral rate for the previous year for the same area was 6.8 per 1,000 population. It seems, therefore, that the existence of this sort of service means that more people are referred to the psychiatrist by the general practitioners. We feel that this is a better measure of the psychiatric service provided to the community than the admission rate to hospital. The latter may, in part at any rate, be determined by such factors as the standing of any particular hospital in the eyes of the local community.

614 or 73% of the patients referred were treated as out-patients in the Day Hospital or at home. In Worthing in 1957 there was a referral rate of 8 per 1,000 of whom 79% were treated out of hospital; the figures for 1958 were 7.6 per 1,000 and 80% respectively.

In 1957 there were 463 admissions from the area covered by the Chichester Scheme. The

number of admissions from this area in 1958 was 228, which gives a reduction of 51%. As was expected, the greatest reduction was in admissions to Summersdale Hospital, the non-statutory unit which caters essentially for the short-stay patient. The admissions to this unit were reduced by 72%. The admissions to Graylingwell Hospital were reduced by 25%. It is perhaps relevant here to state that there are no other psychiatric beds, e.g. observation ward beds, in this area.

Table I shows the number of patients in the different diagnostic categories.

TABLE I

	Male	Female	Total
Affective psychosis ..	105	221	326
Schizophrenia ..	17	29	46
Organic ..	55	83	138
Neurosis ..	61	139	200
Epilepsy ..	13	6	19
Psychopathy ..	7	4	11
Mentally defective ..	6	2	8
Others ..	51	43	94
	315	527	842

In each case we recorded the main factor which determined admission (Table II).

TABLE II

<i>Clinical</i>			
Disturbed behaviour ..	..	..	107
Poor physical state ..	..	..	16
Suicidal risk ..	..	..	13
Patient unco-operative ..	..	..	11
For investigation ..	..	..	9
Stabilization of epileptic fits ..	..	..	2
			158
<i>Social</i>			
Request of relatives ..	..	..	20
To give relatives a rest ..	..	..	17
Living alone ..	..	..	16
Direct request of patient or general practitioner ..	..	..	4
Distance from hospital ..	..	..	2
Bad home conditions ..	..	..	1
Condition of residence (Magistrate) ..	..	..	1
			61
Transfer from Summersdale Hospital to Graylingwell Hospital ..	..	..	9
			228

In 158 patients, admission to hospital was decided on clinical grounds and in 61 patients admission was arranged because of the home circumstances or the attitude of the patient or the relative.

In order to inquire further into the factors determining admission in these 228 patients it was decided to compare the admissions over the six-month period April-September 1958 with the admissions during the same six months in 1957. Table III shows that there are significant

TABLE III

Age	No. of admissions		% change
	Apr.-Sept. 1957	Apr.-Sept. 1958	
0-24	8	7	-12.5
25-44	38	18	-52.6
45-64	73	24	-67.1
65-74	40	26	-35.0
75+	21	27	+28.6
	180	102	-43.3%

$$\chi^2=15.11. \quad P<0.01.$$

changes in the age distribution of admissions in 1958. There is an overall decrease of 43.3%. There is a proportionately greater decrease in ages 25-44 and 45-64. There is an increase (28.6%) in those aged 75 and over. There was a significantly greater decrease in male than in female admissions, the percentage change being 51.7% and 39.8% respectively.

Distance from the hospital was also a factor in determining admission. For those living in Chichester and in the Chichester Rural District Area, which extends some 8-10 miles from the hospital, the decrease was 54.6% and for those living in the rest of the area the decrease was 13.9%. The northern boundary of the area covered by this scheme is approximately 20-22 miles from the hospital. That part of West Sussex is thinly populated. If, however, there were a large centre of population at that distance it would be preferable to open a day hospital and treatment centre there rather than attempt to bring a large number of patients to the Day Hospital at Summersdale.

TABLE IV.—CIVIL STATUS

	1957	1958	% change
Single ..	53	29	-45.3
Married ..	93	37	-60.2
Widowed ..	26	30	+15.4
Separated ..	9	5	-44.4
	181	101	

$$\chi^2=9.12. \quad P<0.05.$$

There is a significant change in the categories of civil status during the two periods under review (Table IV). The decrease in the proportion of married is greater than that of single and separated and there is an increase in the admissions of widows. The social class to which the patients belong also plays a part in determining admission to hospital. The percentage decreases in the different social classes of the two groups were: Classes I and II, 45%; Class III, 49%; Classes IV and V, 32%. There is a pro-

portionately smaller decrease in classes IV and V, but these differences are not significant.

TABLE V.—MODE OF LIVING

	1957	1958	% change
With family	84	48	-42.9
1. With parents	23	13	-43.5
With other relatives ..	18	11	-38.9
2. Alone ..	44	30	-31.8
	169	102	

$$1 \text{ and } 2) \chi^2=0.37.$$

Table V shows the effect of the mode of living. The decrease in admission in those living with parents and family is greater than in those living with other relatives. The least change, 31.8%, occurred in those living alone. These differences are not significant.

TABLE VI

	1957	1958	% decrease or increase 1958/1957
Schizophrenia ..	27	17	-37%
Affective psychoses ..	82	46	-44%
Neuroses ..	32	5	-84%
Senile psychoses ..	18	26	+44%
Other ..	19	8	-58%
	178	102	

$$\chi^2=18.7. \quad P<0.001.$$

There are changes in the admission rates in the different diagnostic categories (see Table VI). There is a highly significant difference in the pattern of admissions in the different groups in the two years. The greatest decrease is in the neuroses. The affective psychoses and schizophrenia also decreased considerably, but there is an increase in the case of senile psychoses—an unexpected finding. It is possible that, because of the facilities provided by this service, especially in domiciliary visiting, more senile patients were referred to us. Nearly all of this increase occurred during the first six months of 1958.

TABLE VII

	1957	1958	% change
Previous admissions (to any hospital)	116	54	-53.4
First admission ..	42	41	-2.4
	158	95	

$$\chi^2=7.38. \quad P<0.01.$$

	1957	1958	% change
Previous admissions (to Graylingwell Hospital) ..	106	40	-62.3
First admission ..	42	41	-2.4
	148	81	

$$\chi^2=11.20. \quad P<0.001.$$

Table VII shows the percentage change in admissions in 1958 as compared to 1957 (a) when there had been a previous admission to Grayling-

well or any other hospital and (b) in the case of first admission. There is a significantly greater decrease in patients with a history of a previous admission to any mental hospital and this decrease is even more marked in patients with a history of a previous admission to this hospital.

It might be expected that with the decrease in the admission of patients suffering from neurosis and uncomplicated affective illness and with the increased admissions of senile psychotics, that the duration of stay of the patients admitted in 1958 would be increased. In 1957 the mean stay in weeks was 8.6 and in 1958 it was 10: this increase is not significant.

It seems therefore that the patient who is most likely to require admission is the widow who is over 75 and who lives alone at a distance from the hospital. She belongs to social class IV or V, she is suffering from senile dementia and she has not had a previous admission to a mental hospital.

The patient who is least likely to require admission is a married man in the age group 45-64 who is living with his family near the hospital. He is in social class III, he is suffering

from a neurotic illness and he has had a previous admission.

We had been kept fully informed of the progress of the original scheme in Worthing during 1957, and we were able to profit from the experience gained there during that year. As a result, it seemed likely that the introduction of a similar scheme would result in a significant reduction in the number of admissions to this hospital from the Chichester area. We were able, therefore, to think of this service in terms of a community service and we were impressed by the flexibility of approach which it allowed. A decision could be made on clinical and on social grounds to treat the patient in hospital, in the Day Hospital, in the out-patient department or in his own home. Each psychiatrist worked in all these fields and he could provide a continuity of treatment when the patient required admission to hospital. Similarly, on discharge the follow-up was carried on by the psychiatrist who had seen the patient in the first instance.

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### Observations on Epileptics in a Mental Hospital<sup>1</sup>

By JOHN TOWERS, D.M., D.P.M.

*Chichester*

THIS study of the long-stay epileptic population of a mental hospital was made for two main reasons—firstly to confirm or refute the high incidence of temporal lobe epilepsy reported among mental hospital epileptics and, secondly, to look for clinical features which might distinguish these epileptics from others in the general population. Investigations such as this have been reported before, notably by Liddell (1953), but I have arranged the material in a slightly different manner and added an additional electroencephalographic (EEG) investigation, namely the use of sphenoidal electrodes and Pentothal-induced sleep. Information about the clinical history was obtained from the case records, some going back thirty years or more, from the nursing staff, and from relatives where they were available. The clinical findings, therefore, are based on a review of the whole of the patient's illness.

Excluding 4 patients who had been in the hospital less than a year and 9 whose fits were presumed to have followed a leucotomy operation, there were, on January 1, 1956, 52 patients who had had at least two major epileptic fits in the previous ten years. This is almost 6% of

the hospital population, about the same as the national average for mental hospitals and, interestingly enough, Hughlings Jackson writing in 1875 reported the same figure. Assuming the incidence of epilepsy among the general public to be one in two hundred, this means that between 4% and 5% of all epileptics are resident in mental hospitals.

Out of the 52 patients here, there were 18 in whom the epilepsy was incidental to another disorder which of itself necessitated mental hospital treatment. There were 8 patients, for example, where it was due to a known or suspected organic brain disease such as senile and presenile dementia and post-encephalitic disorder. In the other 10 patients the epilepsy was incidental to a psychosis: melancholia in 2 cases, manic-depressive psychosis in 3 and schizophrenia in 5. In all 10 patients the psychosis was well established before the fits began. In this group of 18 cases, the average age of onset of the epilepsy was 53 years and the fits in most cases were generalized major convulsions with little in the way of prodromal symptoms or post-ictal phenomena.

EEGs were done in 17 of the patients in this

<sup>1</sup>Being part of work carried out for, and successful in, the South West Metropolitan Regional Hospital Board's 1957 competition for Research Reports.

group. 4 were considered to be within normal limits, 10 showed generalized and symmetrical abnormal activity and the remaining 3 showed focal abnormalities. In 1 of these, the focus was in the left frontal region and was found subsequently to be due to a glioma. The other 2 showed left temporal foci. One of them was a case of presenile dementia who had been fully investigated at a neurosurgical centre where no abnormality was found other than cortical atrophy. The other was a chronic schizophrenic and unfortunately his disturbed mental state precluded the use of sphenoidal electrodes. This investigation was, however, carried out on 6 of the 10 psychotics with incidental epilepsy and in none of them was there evidence of a discharging temporal focus. Thus out of this group of 18 there was only 1 in whom there was suggestive evidence that the fits were due to a lesion in the temporal areas.

The other group of 34 cases were patients whose epilepsy with associated behaviour disorder was the sole reason for their being in a mental hospital and it is with this group that the investigation was mainly concerned. 9 of them were mental defectives at idiot or imbecile level.

#### *Clinical Findings*

It was impossible to obtain information about the early life of 8 patients; in the remaining 26 there was a history of possible birth trauma, either prolonged labour or instrumental delivery, in 6; a history suggestive of neurological illness in childhood in 7 (2 associated with measles and 3 others had convulsions while teething or with whooping-cough); and a history of head injury necessitating admission to hospital in 2. There was, therefore, possible brain damage in childhood in 15 out of 26 patients.

The age of onset of fits varied from shortly after birth to 21 years, an average of 10.4 years. 6 of the 9 mental defectives had begun to have fits before the age of 2 and if all the defectives are excluded, the average age of onset was 12.3 years. The age of admission to hospital varied from 10 to 60 years, an average of 26.8 years. 4 patients, all mental defectives, were admitted under the age of 16. At the other end of the scale, 3 of the 5 patients who were admitted over the age of 40 had been in private nursing care. 28 of the group were certified on admission, either on Urgency or Summary Reception Orders and the other 6 were Voluntary Patients.

Violently disturbed behaviour was the commonest reason for admission but delusions and hallucinations were noted on the certificates of 12 patients and there were attempts at suicide in 6.

For a description of the fits themselves, I am

largely indebted to the nursing staff. This took some time to elicit for it is the usual practice in mental hospitals to describe any form of epileptic activity other than a major convulsion as *petit mal*. All the patients had major seizures and on their clinical form they could be divided up as follows: *Grand mal*, defined as a sudden symmetrically-developing major convulsion in 8 cases; *grand mal* and *petit mal*, defined as a brief interruption in the stream of consciousness noted by an observer as a vacant expression or a suspension of directed activity—in 2 cases; and focal seizures in which a motor, sensory, autonomic or psychical phenomenon was an initial or important symptom in 24 cases.

Prodromal symptoms and signs were recognizable in 17 of the 34 cases—usually increased irritability and restlessness over two or three days. It is probable that 20 patients experienced an aura before their attacks. 13 admitted doing so—auras such as abdominal sensations, giddiness or simply "feeling queer", and in the other 7 there was a noticeable alteration in behaviour immediately before a fit. 4 of them would stop whatever they were doing and lie down on a bed or a convenient chair. An aura used to be thought to be rare among mental hospital epileptics (White, 1900) but in this series just over half the patients had one, about the same as the generally accepted figure for epileptics as a whole. Motor phenomena were observed in 14 patients—such things as myoclonic jerks, munching movements, adverse seizures and automatic behaviour. Automatism occurred in 10 cases, the most commonly observed activity consisting of rearrangement of clothing or dressing and undressing. Of different quality is the epileptic furor—violent and destructive behaviour following a major convulsion—which was recorded in the notes of 15 patients but in only 4 was it a regular occurrence. Another common feature of this group was the epileptic twilight state—a psychotic condition following one, or more often a number of fits, either *grand mal* or focal seizures. This had occurred in 23 patients, just over two-thirds of the group, at one time or other and it was responsible for the admission of 12 of them. In the twilight state, which lasted from a few days to several weeks, there was usually evidence of general toxicity—some were very restless, others very retarded but some degree of perplexity was invariable, as were delusions and hallucinations. These last took various forms but it was striking how frequently they had a religious content, seeing crosses in the sky or hearing the voice of God or the angels. It was not uncommon for the belief in the existence of these hallucinations to persist for some weeks after the toxic phase had passed.

The frequency of the fits of all sorts was reviewed over a ten-year period in 27 of these patients, and the yearly number had increased in 1 case, remained roughly the same in 10 cases and had decreased in 16. 15 out of the total group of 34 had had one or more episodes of status epilepticus.

#### Psychological Aspects

9 patients, as already stated, were mental defectives, 1 at idiot level and the other 8 at imbecile level. A vocabulary test given to 20 patients gave results equivalent to intelligence quotients varying from 59 to 118 with an average of 85. For a rough assessment of personality, the nursing reports in the case records were studied and the nurses' opinion sought on the presence or absence of the following traits—irritability, aggressiveness, impulsiveness, self-centredness, hypochondriasis and religiosity. 19 patients seemed to possess three or more of these traits to a marked degree and they did not appear to be related to the length of stay in hospital, or to an early age of onset of fits, or to the type of fit. Dementia was assessed clinically and was adjudged to be present in 6 patients where retardation and perseveration were prominent and consistent features. In 5 of them it amounted to little more than a bovine slowness but one patient was totally disorientated and incontinent.

#### EEG Investigation

The EEG investigation consisted of ordinary scalp recordings, an average of three per patient, and then a recording using sphenoidal electrodes and Pentothal. It was impossible to obtain records on 2 male defectives because of lack of co-operation but the scalp EEGs of all the other 32 were considered to be abnormal. In 18 the abnormalities were generalized and in 14 were focal, in the form of spike discharges or waves of less than four cycles per second with phase reversal about a common electrode. The distribution of these foci was: over one hemisphere in 2 cases, frontal in 2 cases and temporal in 10 cases, unilateral in 9 of them and bilateral in 1. From scalp recordings, therefore, 10 out of the 32 patients or 31% showed discharges from the temporal areas.

Recordings with sphenoidal electrodes were attempted in 32 patients and were successful in all but one. The value of this procedure is shown by the fact that temporal foci were found in 24 of the 31 cases examined, 77%. They were distributed as follows: Anterior temporal foci—that is spike foci with a phase reversal at the sphenoidal electrode—in 20 cases, bilateral in 13; superficial temporal foci—where the spikes

originated from the middle or posterior part of the temporal lobe—in 4 cases.

In the remaining 7 patients, the use of sphenoidal electrodes did not contribute anything of value.

TABLE I.—CORRELATION OF CLINICAL AND EEG FINDINGS

	Temporal foci	Non-temporal	Total
Prodromata	11	6	17
Aura	18	2	20
Automatism	9	1	10
Furor	12	3	15
Twilight state	18	5	23

When these results are correlated with the clinical findings (Table I) it is found, as might be expected, that there is a high correlation between temporal foci and the presence of an aura and automatism. There is less association in the case of prodromal symptoms, furor and twilight states. From the psychological aspect (Table II) it can be seen that temporal foci were found in 5 out of 7 mental defectives examined and that epileptic personality traits are not exclusive to patients with temporal foci. All the patients showing clinical evidence of dementia had temporal foci but the numbers are too small to draw any definite conclusion.

TABLE II.—CORRELATION OF PSYCHOLOGICAL AND EEG FINDINGS

	Temporal foci	Non-temporal	Total
Mental defectives	5	4	9
"Epileptic" personality	13	6	19
Dementia	6	—	6

It is worth pointing out that most of these patients are not admitted to hospital until ten to twenty years after the onset of their fits—in other words it seems to take some time for the behaviour disorder which causes admission to a mental hospital to develop. None of the patients in this series has in fact been referred for a surgical opinion, as in nearly all the fits are well controlled by anticonvulsant drugs and, just as the frequency of the fits lessens as time goes on, so do the behaviour disorders tend to improve. The question of discharge becomes a social rather than a medical problem. It might be that if investigations with a view to possible surgery could be carried out before disturbed behaviour became well established some at least might be saved the long sojourn in a mental hospital.

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# Social and Familial Correlates of Schizophrenic Delusions [Summary]

By C. J. LUCAS, M.R.C.P., D.P.M.

Chichester

**Background.**—(1) There is little doubt that environmental factors have some influence on the incidence and prevalence of schizophrenia (Slater, 1953; Faris and Dunham, 1939; Hollingshead and Redlich, 1958; Gerard and Siegel, 1950). (2) There is evidence that the clinical form of the illness is affected by environmental factors. Observations have been made on the differences between delusions in certain groups of populations (Sherman and Sherman, 1934; Tooth, 1950; Carothers, 1953; Stainbrook, 1952). Some of the suggestions made by these investigators are as follows: (1) More primitive and less educated people make delusional formulations in religious and supernatural terms. The more sophisticated people "secularize" their delusions (Sherman, Tooth, Stainbrook). (2) Isolation fosters paranoid ideas (Sherman). (3) Low educational status fosters paranoid ideas (Sherman). (4) European education, or its equivalent, in Africans fosters paranoid trends (Carothers). (5) College education fosters grandiose ideas (Sherman). (6) "Aggressive" culture fosters grandiose ideas (Tooth).

**Aims of present study:** To determine in a sample of our own society whether social factors could be related to categories of delusion; such a relationship, if present, would be contributory to an understanding of the interaction between the patient and his social environment.

**Method.**—(1) *Population:* This consisted of male and female in-patients diagnosed by the consultant in charge of the case as schizophrenic. All the male in-patients available in the first half of 1958 were seen and an approximately equal number of female patients who were taken alphabetically on account of their excess in number. (2) *Sources of data:* (a) Delusions: These were studied from hospital records, clinical interview, and reports of sisters, charge nurses and relatives. They were put into the following categories: Religious and supernatural, grandiose, paranoid, sexual, hypochondriacal, inferiority and various (deluded but not fitting the other categories). Patients could have more than one category. (b) Social and familial data were obtained from hospital records, social reports, from a form sent to all relatives, and from interviews with relatives.

**Results.**—288 of 405 patients were deluded. The frequency of the different categories of delusions amongst them was: Paranoid (71%),

grandiose (44%), sexual (44%), religious (21%), hypochondriacal (20%), inferiority (12%), various (8%).

## The Relationship of Categories of Delusion to Age of Onset, Sex, and Social Factors

**Age of onset.**—Among deluded patients, the percentage of paranoid categories rose steadily with increasing age of onset. Other categories, however, showed no clear relationship to age of onset.

**Sex.**—A comparison of categories of delusion is shown in Table I. The outstanding difference

TABLE I.—CATEGORIES OF DELUSIONS AND SEX

	Males N=127	Females N=161	$\chi^2$	P
Religious	18%	24%		
Grandiose	41%	47%		
Paranoid	73%	70%		
Sexual	30%	55%	17.65	0.001
Hypochondriacal	19%	21%		
Inferiority	16%	9%	3.40	0.1
Various	2%	12%	9.77	0.01

between the sexes is the very significantly greater incidence of sexual delusions in women. They also have more various delusions. Males have nearly twice as many delusions of inferiority but the difference is not quite significant statistically.

**Marital status.**—This was taken as that at the onset of the illness. There were 100 ever-married and 188 single persons. The incidence of religious delusions was 25% in the single and 14% in the ever-married ( $P < 0.01$ ). Sexual delusions were more frequent in the ever-married (51%) than in the single (40%), although this difference was not significant statistically.

**Social class.**—Classification of people by social class showed a gradient in the relation of both religious and grandiose delusions and class, not quite reaching the 0.05 level in the case of grandiose delusions. The trend of delusions of inferiority was in the opposite direction, lowest in class I and II and highest in class IV and V (Table II).

TABLE II.—CATEGORIES OF DELUSIONS AND SOCIAL CLASS

	R. G. Social Class			$\chi^2$	P
	I and II N=70	III N=124	IV and V N=89		
Religious	31%	23%	12%	8.56	0.02
Grandiose	51%	45%	34%	4.7	0.1
Paranoid	73%	72%	70%		
Sexual	44%	48%	37%		
Hypochondriacal	23%	23%	17%		
Inferiority	9%	12%	15%		
Various	6%	13%	3%	6.85	0.05

**Educational status.**—To complement class trends patients were examined by educational status. They were divided into two groups. "High status" (independent, grammar or high school, and/or technical or university education); "Low status" (primary, elementary or institutional education). All but 31 could be classified. Differences similar to the class trends were shown (Table III). The greater incidence of

TABLE III.—DELUSIONAL CATEGORIES AND EDUCATIONAL STATUS

	High status N=94	Low status N=163	$\chi^2$	P
Religious ..	28%	18%	2.73	0.01
Grandiose ..	54%	37%	7.40	
Paranoid ..	69%	72%		
Inferiority ..	11%	14%		

grandiose delusions in persons of higher education status is significant.

**Domicile.**—164 of the deluded patients were living in Sussex at the onset of their illness. They could be divided into those born in Sussex (natives) and those from elsewhere (immigrants). These two groups differed in respect of paranoid delusions. Natives (N=82) 67% paranoid; immigrants (N=82) 83% paranoid ( $P<0.02$ ). When examined this difference appeared to be due to females over 30, of whom there were a disproportionate number amongst the immigrants. These immigrant females, ranging in age from 30 to 60 or over at onset were more paranoid than native females in the same age range (Table IV).

TABLE IV.—PARANOID DELUSIONS AMONGST NATIVE AND IMMIGRANT FEMALES OVER 30 AT ONSET

	Natives N=15	Immigrants N=43	$\chi^2$	P
Paranoid ..	66%	93%	4.47	0.05

**Sibling position.**—Grandiose and paranoid categories differed among siblings of different positions (Table V). There were more paranoid

TABLE V.—DELUSIONS AND SIBLINGS POSITION

	Eldest N=65	Youngest N=71	Only N=18
Paranoid ..	55%	78% (a)	83%
Grandiose ..	51%	34% (b)	44%
(a) Paranoid eldest v. youngest $\chi^2=7.47$ ( $P<0.01$ )			
(b) Grandiose eldest v. youngest $\chi^2=4.0$ ( $P<0.05$ )			

delusions in youngest and only children, and fewer in eldest children. In contrast, grandiose delusions were commoner in the eldest.

The categories of delusion were also examined by breaking down their content further. It was found that the commonest type of sexual delusion was a false belief of imposed heterosexual activity. Women more often had false beliefs of marriage (and pregnancy) and these were as

common in the ever married as in the single. In men, such beliefs favoured the single. None of the women, in contrast to the men, had delusions centering around masturbation.

Grandiose delusions were subdivided into delusions of authority and power, of wealth, of social status, and of special skill or ability. No class difference was demonstrable, but there was a greater incidence of delusions of power and authority in men (27%) compared with women (4%) ( $P<0.001$ ).

Paranoid delusions were subdivided in terms of persecuting agency. Class I and II persons named more varied persecutors (such as Jews, Freemasons, Communists, Blackmen) in contrast to class IV and V persons who more commonly cited the police.

From the trends observed, the kind of pattern which seemed to emerge was that there may be a more direct translation of social role and position into delusional terms than is usually envisaged. Rather than the lowly and inferior compensating with delusions of grandeur, and the sexually deprived having sexual delusions, it is the opposite that seems to occur. It is the better educated, the higher class, the eldest of the family who tend to be more grandiose, the lowly who are more inferior, and the sexually experienced who have more sexual delusions. In other words, the more simple and obvious hypotheses relating social factors and delusional symptoms appear to be those most worth testing.

The findings will be reported and discussed in detail elsewhere.

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<sup>1</sup> Fowler, E. P. Ann. Otorhinolaryng., 1950, 59, 980.

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### OTOLOGICAL SESSION

#### SYMPOSIUM ON FACIAL PARALYSIS

Dr. Karsten Kettel (Hillerød, Denmark):

*Management of Peripheral Facial Palsies due to  
Trauma*

#### INTRODUCTION

For twenty years the surgical treatment of peripheral facial palsies has been a favourite interest of mine.

Since Bunnell, Robert C. Martin and Ballance and Duel a quarter of a century ago introduced modern facial nerve surgery, enormous progress has been made and wonderful results obtained all over the world, due to one simple fact: *The pioneers changed the principle of the therapy. Hitherto* one had to be content with such help as could be had from neurotizations and anastomosis operations and in successful cases that meant (1) a good tonus with the face at rest and (2) the ability to perform voluntary movements *but no more*. Now, we can obtain not only good tonus and voluntary movement but, and this is the essential thing, *emotional* control of the facial muscles.

The symmetry and synchronism of the emotional movements of the face are dependent on the close co-operation of the cortical facial centres of both hemispheres, and the only way to re-establish this cortical interplay in cases of peripheral facial palsy is to repair the injured nerve at the site of the lesion.

This is why direct repair of the facial nerve at the site of the lesion is superior to any other procedure in the treatment of peripheral facial palsies, a postulation which recently has been criticized by Martin and Helsper (1957). The purpose of their paper is "to present clinical evidence that following surgical section and sacrifice of a considerable segment of the VII cranial nerve (including a portion of its main trunk and the peripheral plexus) there can be spontaneous recovery of function in a fair percentage of cases without resort to nerve grafting or any other form of neurotaphy".

Martin and Helsper postulate that "it seems reasonable to conjecture that following complete and permanent interruption of the motor pathway through the VII cranial nerve, voluntary motor impulses by re-education may find their way from the cortex through the V cranial nerve to the respective muscles".

This statement is in flagrant contradiction to all physiological and neurological laws hitherto accepted, though of course this does not necessarily imply that it is wrong. However, I agree with the authors when they say: "We have been unable to find any previous report of recognized spontaneous recovery of function following segmental operative defects of the VII cranial nerve in adults."

40 of their patients "had a deliberate section of the VII cranial nerve and an excision of a segment of between 2.5 and 5 cm. of the main trunk of the nerve and its peripherally extending branches (plexus)". 28 lived long enough so that it could be established that "at least 8 patients (28.5%) had a fair degree of return of function in the paralysed facial musculature without resort to nerve grafting or any other reparative operation".

What did Martin and Helsper really observe? According to their paper they have obtained a beautiful tonus with the face at rest and the ability to perform very limited *voluntary* movement indeed. This may be valuable; but *emotional* movements, the goal of our therapy, have not been restored.

How do the authors explain their observations?

They call attention to the fact that "there are elaborate anastomoses (plexuses) between the terminal branches of the V and VII cranial nerves in all parts of the facial musculature from the forehead to the lower lip" and they believe "that new motor pathways are established through the V cranial nerve".

They do not think that a spontaneous regrowth

of VII cranial motor nerve fibres across a defect of several centimetres has taken place, because then a re-excision of the parotid area for carcinomatous recurrences would be followed by loss of what spontaneous movements had been obtained, and it was not so. The authors also reject the possibility of a decussation and/or anastomosis across the mid-line of the face, and they conclude that what re-innervation they have observed is due to communications or anastomoses of the terminal branches of the V cranial nerve within the terminal branches of the VII cranial nerve.

The authors also suggest another explanation of their observations: "What at first may seem to be merely an additional minor anatomical detail may actually also have considerable significance. The masticator nerve (V cranial) is known to contain both motor and sensory fibres. Its buccinator branch (which according to Cunningham is only sensory) perforates the buccinator muscle before supplying sensation to the skin and mucous membranes of the cheek. The significant question is whether or not the latter supposedly only sensory nerve might also carry some dormant motor fibres which are given off as the nerve pierces the buccinator muscle. If such were the case, there would be a reasonable explanation for the fact that in our 8 cases a voluntary drawing back of the angle of the mouth (by buccinator contraction?) has invariably been the first sign of recovery."

I may add that the possibility of a decussation and/or anastomoses across the mid-line should not be entirely rejected. I once performed a nerve grafting on the left side, including the horizontal, vertical and part of the extratemporal segments of the facial nerve. Before, as well as after, the nerve grafting the patient could perform some small movements at the side of the nose and on the chin, but these movements disappeared immediately when the right (sound) facial nerve was anesthetized at the exit from the stylomastoid foramen, to reappear when the effect of the procaine had stopped.

As to the possibility that re-innervation observed by Martin and Helsper should be due to dormant motor fibres in a supposedly sensory nerve, Buchthal, who is professor of neurophysiology in Copenhagen, points out that it is more likely that the motor branch of the trigeminal nerve has been injured in removing the tumour of the parotid gland and then starts "sprouting" eventually to innervate a small group of the facial muscles.

Finally Martin and Helsper conclude that it seems reasonable that motor impulses reach the muscles by re-education through the V cranial

nerve and they state: "We question the justification for any form of neuroorrhaphy or extensive plastic repair (except eyelid fusion) for VII cranial nerve paralysis due to operative defects until at least a year or more has passed. We submit, furthermore, that in view of the fact that spontaneous recovery has taken place in over one-fourth of our cases, there is considerable doubt that any of the few recoveries, as reported in the literature, following neuroorrhaphy, are actually due to that cause."

In the interest of the patients suffering from a traumatic defect of the facial nerve, I consider it my duty to ask the following questions.

If Martin and Helsper were right, (1) Why have I never seen any signs of tonus or spontaneous recovery in post-operative facial palsies in which the nerve has been severed and not repaired? (2) Why has the outcome been exactly the same in the many patients referred to me in which the palsy was due to the removal of a parotid tumour? (3) Why did I not get any result in the patients in whom I tried to repair the nerve but for various reasons was unable to do so, with an ensuing permanent palsy and lack of tonus? Why on the other hand were clinically satisfactory emotional movements obtained in 90% of patients in whom the repair was successfully done? These were not merely limited and isolated voluntary movements. (4) Why did the good emotional movements which I had obtained in one of my patients by nerve grafting disappear immediately when the radical cavity years later was cleaned elsewhere, and the graft accidentally removed? (5) Why are the experiences of Cawthorne, Sullivan and Jongkees in complete accordance with mine?

I think that the explanation is that there is one way and one way only to obtain emotional movements of the face when the facial nerve has been damaged, and that is to re-establish next-to-normal physiological conditions by repairing the nerve at the site of lesion. Only through a nerve graft or a nerve suture can neurofibrils originating in the facial nucleus reach the muscles supplied by the facial nerve, and only through these channels will impulses reach the facial muscles and restore emotional control of the face.

For these reasons I consider it is my duty to oppose any statement to the effect that repair of an injured facial nerve should be postponed in favour of expecting "that the motor pathways to the facial musculature are re-established by way of the V cranial nerve" (Martin and Helsper).

As already stated, I do not doubt the observations made by Martin and Helsper, but even if they are interesting from the physiological point of view, they are without any clinical value at all,

now we are able to repair an injured facial nerve properly.

If the facial nerve is severed it should be repaired at the site of the lesion as soon as possible.

I cannot express the truth as it seems to me better than by quoting Ballance and Duel. "The accepted time to operate is now. No delay is justifiable."

#### **PATHOLOGY**

A traumatic facial palsy may be due to (1) operative lesions and (2) external violence, and the nerve may suffer one of three grades of damage:

(a) *Neuropraxia*.—This is the slightest degree of damage to the nerve as only the myelin sheaths are affected, neither the neural elements nor the supporting sheaths being affected. An example is the palsy which occurs some days after the accident and which disappears spontaneously and completely.

(b) *Axonotmesis*.—Here the neural elements are separated from the nutrient nerve cell and degeneration of axons and myelin sheaths will take place distal to the site of injury. The neurilemmal sheaths, however, are not interrupted and the patient may make a spontaneous but incomplete recovery. In fractures of the facial canal without interruption of the continuity of the nerve axonotmesis may be present.

(c) *Neurotmesis*.—Here the neural elements as well as the nerve sheaths are completely interrupted due to either operative lesions or external violence.

#### **SURGERY**

To deal with the pathological conditions three operative procedures are at our disposal, and it may be mentioned that now we are able to repair the facial nerve along its entire peripheral course.

(1) *Decompression of the facial nerve*.—By this procedure the facial canal is opened and the aim of the operation is either (a) to relieve a pressure upon the nerve due to an oedema or an intracanalicular hæmorrhage, a pressure which initially has caused a neuropraxia but if not relieved in time may lead to an axonotmesis or, in the severest cases to a neurotmesis, or (b) to remove bone splinters impinging upon the nerve. Finally, (c) decompression may be the first step in accomplishing nerve grafting or nerve suture.

(2) *Nerve grafting* and

(3) *Nerve suture*.—In some cases the course of the nerve is shortened by "re-routing" it according to Bunnell.

These operations are so well known and so well established that they need no further comments.

#### **CLASSIFICATION OF CASES**

The facial nerve may be injured intracranially, intratemporally and extratemporally.

##### **A. INTRACRANIAL LESIONS OF THE FACIAL NERVE**

These may be due to external violence, as in some cases of fractures of the skull, as well as to operative traumas, especially following removal of acoustic neurinomas.

Previously, one had to resort to anastomosis operations or, if these failed, to plastic operations.

Now it has been made possible to repair the nerve directly thanks to Professor Norman M. Dott. He has described an operation in which the temporal bone is "by-passed". The proximal end of the facial nerve is sutured to a nerve graft 15 cm. long. This is brought out through the occipital craniotomy opening, thrust forward through a tunnel beneath the mastoid process between the sternomastoid and splenius capitis muscles. Distal to the stylomastoid foramen the facial nerve is cut. The distal end of the graft is at this place sutured to the distal end of the facial nerve.

The indications for Dott's operation are intracranial lesions of the facial nerve, as well as intratemporal lesions in cases in which the temporal bone is destroyed and intratemporal nerve grafting cannot be accomplished. Dott has obtained excellent results with his operation.

##### **B. INTRATEMPORAL LESIONS OF THE FACIAL NERVE**

These may be due to external violence, as well as to mishap in otological operations. It is, of course, of the utmost importance to distinguish between two groups of palsies according to the time of onset:

(a) *Palsies arising in direct conjunction with the accident*.—In such cases the continuity of the nerve may be interrupted, but not necessarily so.

(b) *Palsies of delayed onset*.—It should be remembered that in palsies due, for example, to external violence it may be difficult to tell the exact moment when the palsy started due to lesions of the soft tissues of the face.

However, if the palsy really does not start till some time has elapsed, then we know that the continuity of the nerve has not been severed. The palsy may be due to an intracanalicular oedema or hæmorrhage, which may disappear spontaneously, but in some cases the pressure upon the nerve and its vessels within the fallopian canal may lead to degeneration of the nerve if not relieved in time.

### *Post-operative Facial Palsy*

(a) *Palsies arising in direct conjunction with the operation.*—It is obvious that these should be repaired, but when? Miss Collier advocates postponement for about three weeks for two reasons: (1) Infections in the neighbourhood of the graft may lead to intra- or extraneural fibrosis, and (2) the outgrowth of Schwann cells from the peripheral stump towards the centre, which plays the part of a bridge by which the regenerating axons reach the periphery, is most vigorous between fifteen and twenty-five days after division.

Miss Collier may of course be perfectly right but, like Cawthorne and Sullivan, I have always maintained that repair should be undertaken immediately for three reasons: (1) If the nerve really has been cut, the conditions for repair are the best possible immediately after the injury. By postponing the intervention the stumps must be identified and isolated from granulations or scar tissue, which may be difficult, whereas it is very easy just to reopen the wound immediately and to see what has happened. (2) Infection in the cavity is in these antibiotic days of no importance as, according to Sullivan, in most cases we are dealing with a low-grade infection in a chronic otitis media. (3) The surgeon can tell the prognosis immediately and put his own as well as the patient's mind at rest.

Following these lines of reasoning I have performed 70 nerve grafts and 8 nerve sutures.

In 14 cases, practically all extratemporal lesions, the conditions for repair were unfavourable. In many cases I could not find the ramifications of the nerve in the cheek and thus could not complete the operation. In 6 some re-innervation was obtained but clinically this was quite insufficient. In 8 complete failure followed.

In 64 the conditions for repair were favourable. 63 of the patients have been re-examined and a clinically good result was obtained in 57 cases (90%).

The minimum requirement for a case to be classified as favourable is that the patient should look normal with the face at rest and be able to smile.

All patients looked normal with the face at rest; 6 could only smile; 44 could also screw up their eyes and 7 could even wrinkle the forehead a little.

It should be remembered that a 100% cure is never obtained, but I think the results are most gratifying. Without direct repair of the nerve

all the patients would have suffered from a complete and appalling facial palsy for the rest of their lives.

(b) *Palsies of delayed onset.*—Here we know that the continuity of the nerve is not interrupted and the chances of a complete and spontaneous recovery are fair. The palsy may be due to pressure of tampons, to an oedema or a hæmorrhage within the fallopian canal.

I would suggest the following mode of action: If the post-operative palsy is of delayed onset the patients are just observed and decompression performed only if (1) repeated electromyograms show a severe interference with nerve conduction or, for lack of this apparatus, if (2) after two months of observation there are no signs of returning mobility. When the nerve has been uncovered at the site of the lesion, one will have to decide whether decompression is sufficient or whether resection of part of the nerve, which may have degenerated, is indicated with ensuing nerve grafting.

I do not think that there are any problems in the indications for the management of post-operative facial palsies.

Thanks to a heavy reduction of the number of mastoidectomies in these antibiotic days and to a better surgical technique during the last decade, post-operative palsies are becoming less frequent.

The contrary applies to palsies due to fractures of the temporal bone.

### *Facial Palsies due to Fractures of the Temporal Bone*

It has hitherto been considered that practically all these recovered spontaneously, but that is not so, and to-day there is a general agreement between facial nerve surgeons that surgical intervention is needed in selected cases.

#### *Indications for Operative Treatment*

Here again we must divide the palsies into those arising in direct conjunction with the fracture and those of delayed onset.

(a) *Palsies arising in direct conjunction with a fracture of the temporal bone.*—In such cases the nerve may be severed but not necessarily so. They are as stated by Grove (1939) usually due to a lesion of the nerve by the line of fracture usually distal to the geniculate ganglion. An intracanalicular, extra- or intra-neural hæmorrhage, a tearing of the nerve, bone splinters impinging upon the nerve sheath or a compression of the nerve between dislodged fragments may also result in an immediate palsy.

Cawthorne has said that "skull fractures in which facial paralysis is accompanied by signs of

damage to the ear, particularly if the middle ear is affected, should be considered as possible instances of fracture involving the middle ear cleft and the facial nerve as it runs along its inner wall", and moreover "In a case of facial palsy dislocation of the incus as evidenced by conductive deafness and in abnormal appearance of the tympanic membrane is a definite indication for exploration of the nerve trunk in the fallopian canal".

I completely agree with Cawthorne. While a few surgeons are in favour of a conservative treatment in all cases, the majority, including Maxwell, Sullivan, Ersner, Farrior and Caldwell, Behrman, Rowbotham, Grove, Lang, and Wullstein, recommend surgical intervention in selected cases. In cases of immediate and complete paralysis an exploration of the facial nerve should be done as soon as the patient's general state of health permits it, once a definite diagnosis of a severe and accessible lesion of the nerve has been made.

By a severe lesion is to be understood complete conduction block with denervating potentials and fibrillation as indicated electromyographically. If an apparatus for electromyography is not available, I consider any palsy severe which shows no signs of spontaneous improvement within two months of observation, as the favourable cases show signs of improvement within this time limit, and usually within two to three weeks (Rowbotham). Regardless of the results of electrical tests, I would never postpone surgical intervention for more than two months.

This mode of action can be adopted without any risk of impairing the hearing in (a) transverse fractures of the temporal bone, because both vestibular and acoustic functions are lost, and (b) in longitudinal fractures where the nerve is injured in the pyramidal and vertical segments, because exploration can be done without injuring the contents of the middle ear.

If, however, the nerve is injured in the horizontal segment there may be a risk of destroying the middle ear. In some cases, even in this site, the nerve may be repaired without damaging the middle ear (Maxwell and Magielski, Kettel, Wullstein), but, on the other hand, it may be necessary to do a radical mastoidectomy in order to repair the nerve. Needless to say, the patient should be told in advance.

(b) *Palsies of delayed onset.*—In the majority of such cases intracanalicular hæmorrhage or œdema is responsible for the facial palsy. It should be stressed that because of the external lesions of the face, present in many cases, it may be difficult to tell if the palsy is immediate or of delayed onset.

The prognosis is generally fair under a conservative treatment, but in some cases decompression is indicated. I would recommend decompression within two months after the injury, or sooner if serial electromyograms, which should be started early, show a severe interference with nerve conduction. These indications have been adopted by many surgeons.

Previously decompression was not performed in many cases for fear of impairing the hearing but, as proved by many of us, this may be done without touching the ossicles and the drum.

### Results

I have operated upon 18 patients with facial palsy due to a fracture of the temporal bone, all, to the best of my knowledge, developing at the time of the accident.

In 17, the fracture was of the longitudinal type, with an initial impairment of hearing due to a hæmatotympanum. In one a transverse fracture had immediately destroyed the labyrinth. The nerve may be injured in the horizontal segment (3 cases) the pyramidal segment (8 cases) or the vertical segment (4 cases). In 3 nothing abnormal could be observed at operation, but nevertheless in two of them, operated upon two and a half and three and a half months after the accident, movements started immediately after the decompression.

In none of the remaining 15 patients was the nerve severed, but in all of them definite alterations were encountered, ranging from a simple œdema of the nerve to a heavy compression between dislodged fragments.

In none was a complete cure obtained, meaning that not the slightest trace of the palsy was left. However, the results are quite satisfactory as 12 patients had a complete palsy before decompression and 6 an almost complete palsy except for faint contractions at the corner of the mouth, whereas on re-examination of 15 of the patients (one of them with a bilateral palsy) 14 looked completely normal and 13 could screw up their eyes and smile more or less normally. One patient regained a fair movement of the mouth but suffered from a lasting paralysis of the II, IV and VI nerves and one has not been re-examined.

Have these results been obtained on account of or in spite of the operation? In cases where the nerve had been compressed and even dislodged by fragments, the connexion between operation and results is obvious. In cases where œdema or intracanalicular bleeding was observed, the patient might have improved after further delay. But, in my view, it is fair to assume that decompression has hastened recovery, especially when improvement started in direct conjunction with

surgery, or where the spontaneous improvements had long ago stopped far short of complete recovery but started again after decompression.

Could better results have been expected? Under present conditions I believe not, because the majority were operated on at a rather late date. In cases in which the nerve is compressed between displaced fragments, it is obvious that the earlier it is freed, the better the chances of recovery. I think that this line of reasoning also applies to patients in whom the palsy is due to pressure within the facial canal, which in itself does not abolish conduction, but interferes with the nutrition of the nerve, leading to degeneration.

#### C. EXTRACRANIAL LESIONS OF THE FACIAL NERVE

The palsies belonging to this group may be due either to operative lesions or to external violence.

(1) *Operative lesions*.—The majority of these result from removal of the parotid gland. In many cases the gland may be removed without injuring the facial nerve, because the ramifications of the nerve are situated between the superficial and deep lobes of the gland. In other cases (malignant tumours), sacrifice of the nerve is unavoidable if the tumour is to be removed.

(2) *External violence*.—While the number of post-operative facial palsies is decreasing, the frequency of palsies due to external violence is rapidly increasing, not least because of modern traffic.

Whether due to mishap in surgery or to external violence, these palsies should be repaired as soon as possible, and I completely subscribe to Maxwell's indications:

If the patient's general condition permits of a prolonged surgical procedure, the optimum time to repair a damaged facial nerve is at the time of primary repair of the facial laceration. Late repair is sometimes necessary, but the inflammatory changes in the parotid gland render the identification of small branches of the nerve more difficult. It can, however, be accomplished in many instances.

If the facial paralysis is noted immediately after the laceration, and usually it will be, exploration to determine the exact type of injury is indicated. If, for any reason, exploration has been delayed, it must be remembered that the longer the delay the poorer will be the results of repair. Some fibrosis of paralysed facial muscles occurs in a year, after this the change is more rapidly progressive, militating against a good functional result from any type of nerve repair. These words of Maxwell also apply to extratemporal operative palsies.

The results obtained by Maxwell and Lathrop following these indications are excellent. My

own results are poor, but I may add that the majority of cases were not referred to me till years after the damage had been done. It was just impossible for me to isolate the ramifications of the nerve in scar tissue.

In cases of manifest or suspected lesions of the facial nerve in an accessible site, the nerve should be inspected and repaired without undue delay. Suitable operative methods are at our disposal and no delay is justifiable.

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Miss Josephine Collier (London):

*Rationale for Operative Treatment*

The first objective should be a study of the pathological nature of the nerve lesion. This requires examination of the history and recourse, also, to the methods of electrodiagnosis. Such considerations apply equally to facial paralysis following operative injury, fracture of the skull and gunshot wounds and to Bell's palsy.

The history of operative cases should include the surgeon's report of his findings with, perhaps, a note on the absence of landmarks, lost from progressive middle ear disease or from earlier operation. There may be, too, reference to excessive bleeding from granulations in the region of the facial canal. The surgeon sometimes reports his certainty of nerve damage and the precise site. In cases following operation or intracranial fracture it is customary to distinguish between those of immediate onset and those where the appearance of the paralysis is delayed. Undoubtedly the appearance of complete facial paralysis immediately after the injury indicates a destructive lesion. In judging whether the onset was delayed there should, however, be some caution. Facial paralysis may easily be missed in an unconscious patient with a bandaged head and unless the paralysis has specifically been looked for and the state of the facial movements reported in the notes, a history of onset one to two days later cannot be relied upon to give the true picture. I have in my records a number of patients whose paralysis was reported as occurring thirty-six hours or even longer after operation or fracture and where, in point of fact, at the operation on the nerve the divided ends have been found separated, so that complete paralysis must have occurred at the time of the original trauma.

There is another cause of confusion as to the completeness of the paralysis—one that may lead to an erroneous belief that the paralysis did not develop immediately after the operation or fracture. The relaxation of levator palpebrae superioris when the patient is asked to close his eyes is sometimes interpreted as movement of orbicularis oculi and the deduction is made that the nerve must be intact. I have seen conclusions based on faulty observations of this kind lead to failure to diagnose a severe traumatic lesion.

Complete facial paralysis immediately after operative injury is an indication for early exploration. Tests for nerve conduction will confirm the degree of denervation. The extent of nerve damage found will determine the type of reparative operation required—removal of fragments of the bony canal or nerve grafting—but in every case uncovering the whole course of the nerve in

the descending canal is necessary to allow for swelling.

A consideration of the natural history of Bell's palsy is basic in a discussion on the rationale for operation. In most cases the nerve never degenerates but is in a state of neuropraxia or reversible block to conduction and recovers spontaneously and completely. Mixed lesions occur with varying proportions of degenerated fibres. Those fibres that degenerate (few, many or all) can recover only by regeneration, a process that must be protracted since regeneration proceeds at an estimated average of no more than an inch a month. In my experience there is always some regeneration—with, of course, the defects that inevitably accompany degeneration, namely, weakness as compared with the sound side and some degree of mass movements and contractions. I have no record of any patient with true Bell's palsy of many years' duration without some sign of regeneration. The appearance of a patient who has had complete, long-standing facial paralysis is well known. This may be seen after an old mastoid injury or after an operation for an VIII nerve tumour or a parotid tumour when the nerve has been sacrificed. When such a complete paralysis appears to have occurred spontaneously (and has therefore carried the label Bell's palsy) one can generally find grounds for placing the original lesion at or central to the geniculate ganglion, perhaps in the facial nucleus. There may, for example, have been a history of pyrexia and malaise with or preceding the paralysis and this should always arouse suspicion.

My present concern, however, is to discuss how methods of electrodiagnosis may assist in prognosis on which decision for operation should be based. Accurate assessment of the pathological state of the nerve is necessary as a guide to management and as a safeguard for judging the value of any preferred treatment. This applies equally to direct operation on the nerve in traumatic lesions and to decompression or sympathetic nerve block and to medical methods of treatment for Bell's palsy such as steroid therapy.

The objective of the operation, in every type of case, should be clearly understood, whether it is to prevent degeneration or to provide facilities for regeneration. In operative injury, for example, there may be a spicule of bone piercing the nerve. Exploration gives an opportunity of removing the fragment and so allows regeneration of the damaged fibres. It is necessary, however, in addition, to uncover the whole course of the nerve from the site of injury down to the stylo-mastoid foramen to allow for swelling with the

object of preventing degeneration in fibres not directly injured.

There are two critical periods in the course of facial paralysis when exact information on the pathological state of the nerve is especially necessary to serve as a control of any line of treatment. One is the first few days after onset and the other between two and three months later when re-innervation may be impending even though there be no clinical sign of returning movement. During the first two to three days the problem is to determine whether the assault that has been made on the nerve has produced degeneration or merely an interference with conduction of the nerve impulse without breaking up of the axons. At this stage the only test that can give this information requires a stimulator capable of delivering stimuli of measured duration and strength. Such an electrical stimulator (either of constant current or of constant voltage) places nerve testing on a quantitative basis so that the changing state of the nerve can be observed by repeated comparable testing, if necessary from day to day.

One of the difficulties preventing elucidation of the problems of Bell's palsy is the well-known fact that most patients recover within the first few weeks and it is only when recovery is tardy that patients are sent to centres where they can be adequately studied. Most patients reach the otologist between six and ten weeks after onset because the paralysis has not recovered. This is the second critical period for prognosis. The main difference of opinion among otologists on the indications for operation in Bell's palsy relates to this point. Without reliable electrical investigations using the quantitative and exact methods employed in electrophysiology—now much simplified for clinical use—the opinion formed on the state of the nerve is, at this stage, subject to two possible errors. The first is to mistake persisting neuropraxia for a more destructive lesion. Persisting neuropraxia is not a frequent phenomenon. It does, however, occur. I have found complete paralysis without evidence of degeneration up to 11 weeks and others have recorded similar findings. Such conduction block, likely to recover spontaneously at any time, may be responsible for the signs of returning function sometimes seen a few days after decompression operations. For this reason decision for operation should always be supported by precise electrical tests. The state of the nerve—conduction block, degeneration or a mixed lesion—would then be evident and the grounds for operating properly evaluated.

The second error is the possibility of impending re-innervation. Here is the paramount need for

examination by electromyography of patients seen for the first time eight weeks or later after onset of the paralysis, whether the cause be trauma or Bell's palsy. The evidence for re-innervation is the presence of polyphasic motor unit action potentials and the progressive diminution of fibrillation action potentials. It may be obtained many weeks before any facial movements can be detected.

This is the crucial point. Out of a series of 100 cases of varied aetiology 40, first examined between eight and eighteen weeks after onset, were without clinical signs of recovery. There was, however, electromyographical evidence of re-innervation in 26. The examination was repeated at intervals. Increasing electrical evidence of re-innervation was found in as many as 23 and in these satisfactory clinical recovery occurred. 5 cases were the result of intracranial fracture and each one attained a reasonable degree of facial movements without operation. When there is no electromyographical evidence of re-innervation at a date after injury when some re-innervation would be possible exploration should, of course, be undertaken in mastoid cases; decision in intracranial fractures depends, in addition, on anatomical and otological data as to accessibility. This is outside the scope of my present thesis.

It is true electromyography is not always to hand but that fact has no bearing on its efficiency. Further, interpretation requires skill and care. There is, however, no urgency at this stage; a delay of a week or more in seeking tests elsewhere will not affect the issue. The progressive simplification of apparatus designed to be used by those who lack specialized knowledge of electronics is a strong argument for its being more generally available. Otologists should be able to apply to facial nerve surgery the same technical equipment as do others who also deal with lower motor neurons.

Certainly we should not ask of machines more than they can by their nature give. It is necessary to know at each stage when to apply the particular tests and how to interpret them. In the first few days after onset only by testing for nerve conduction by quantitative stimuli can we learn whether a nerve is degenerating. In my experience fibrillation cannot be expected earlier than twelve days. After the fifteenth day intensity-duration curves give more exact information, that is, the degree of denervation and thus, possible evidence of a mixed lesion. Finally, the only method of detecting re-innervation before clinical recovery is examination by electromyography. Once degeneration has occurred nerve conduction remains abnormal for lengthy periods. There is,

however, progressive alteration in the character of intensity-duration curves towards the normal as re-innervation takes place.

I would say, in conclusion, that precise methods of electrodiagnosis are as necessary in the management of facial paralysis as is the audiometer for operations for otosclerosis.

Mr. J. D. Gray (Sheffield) showed a film entitled *Dissection of the Middle Ear, as shown by Zeiss Microscope*.

#### Dr. Deryck Taverner (Leeds):

##### *The Prognosis and Treatment of Spontaneous Facial Palsy*

Although there is an enormous literature about spontaneous facial palsy, we are still quite ignorant of its causation, there is no treatment of proved value and there is little agreement about the prognosis. I shall deal largely with the natural history of the disorder and my remarks on treatment will be devoted mainly to some practical points of management.

This paper results from a personal clinical and electromyographic study of 341 patients with idiopathic facial palsy. The methods used have previously been described (Taverner, 1955). It is generally agreed that the great majority of patients recover completely within two or three months and we assume that they suffer conduction block only. In the remainder denervation sets in, recovery is never complete and various sequelæ occur. There is strong evidence that electromyography and study of the electrical reactions are the best indicators of the outcome, because they show the presence of denervation at an early stage.

In this study patients have been allotted to the two groups of conduction block and denervation mainly on the basis of electrical studies but a few were re-allocated later as a result of follow-up. Errors in initial allocation were found on five occasions which is an error of 1.5% or 1 in 70.

#### *The Findings*

In the whole group of 341 patients 177 suffered conduction block only and recovered completely. The remaining 164 suffered varying degrees of denervation and did not recover completely. They are referred to as CB and D groups of patients respectively.

(1) *Age and sex distribution.*—There were 167 males and 174 females and there was no significant sex difference between the CB group and the D group (Table I).

Type	Total	Male	Female
Conduction block	177	94	83
Denervation	164	73	91
Whole series	341	167	174

The ages of the whole group ranged from 3 to 85 years with a mean of 39.6 years. The mean age of the CB patients was 34.4 years and that of the D group was 44.8 years. Fig. 1 shows histograms of the number of patients in each ten-year age period from 0-10 to 71 upwards in both the CB and D groups. The difference between these groups is statistically highly significant ( $\chi^2=26.99$ ,  $n=7$ ,  $P<0.001$ ). Of the 14 patients up to the age of 10, 13 recovered completely but of the 18 patients over the age of 70 years only 5 recovered completely. Similar but less marked differences were found in the other age groups.

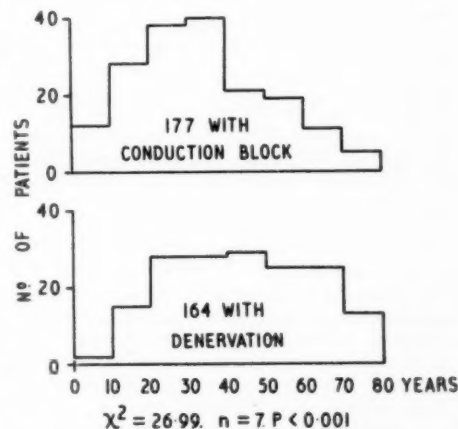


FIG. 1.—Histograms of age distribution in facial palsy.

(2) *The incidence of denervation of the 257 patients who were first seen less than two weeks from the onset of the disorder, at a time when the outcome was still in doubt, is given in Table II.*

Total	Denervation	Conduction block
257	40% (103)	60% (154)

Exactly 60% (154 cases) showed conduction block and 40% developed denervation.

(3) *Clinical guides to prognosis.*—Analysis of the 341 patients in the whole series shows that initial pain and complete paralysis are both significantly more common in the D than the CB groups. 43% of the CB group complained of pain compared with 57.9% of the D group (Table III). The difference between these two

TABLE III.—RELATIONSHIP OF CLINICAL FEATURES TO PROGNOSIS IN FACIAL PALSY

Type	Total	Pain	Taste	Herpes
Conduction block ..	177	43.0%	45.7%	3.0%
Denervation ..	164	57.9%	42.7%	7.9%
Difference ..		-14.9% ( $\pm 5.7$ )	3.0% ( $\pm 5.4$ )	-4.9% ( $\pm 2.46$ )

Figures in brackets indicate S.E. of Difference.

proportions is 14.9% ( $\pm 5.7$ ) which is statistically significant. Table IV shows that only 17.5% of the CB group developed electromyographi-

TABLE IV.—RELATIONSHIP OF DEGREE OF PARALYSIS TO PROGNOSIS IN FACIAL PALSY

Type	Total	Complete palsy
Conduction block ..	165	17.5%
Denervation ..	146	65.1%
Difference ..		-47.6% ( $\pm 4.9$ )

Figures in brackets indicate S.E. of Difference.

cally complete palsy compared with 65.1% of the D group. The difference between these two proportions, of 47.6% ( $\pm 4.9$ ), is highly significant.

A similar calculation for loss of taste, as determined subjectively by the patients, showed no significant difference (Table III) but a herpetic eruption was observed in only 3% of the CB group as opposed to the 7.9% of the D group. The difference between these proportions, of 4.9% ( $\pm 2.46$ ), is on the verge of statistical significance.

(4) *Duration of palsy.*—Movements of the facial muscles began to reappear or to improve 2–21 days after the onset in the CB group and the mean time to the onset of recovery was 10.05 days ( $\pm 0.35$ ). The corresponding figures for the D group were 7–150 days with a mean of 61.8 days ( $\pm 3.24$ ). The difference of these means is significant. Recovery was complete in the CB group in from 10–150 days from onset with a mean of 46.3 days ( $\pm 1.62$ ). The patients in the D group never recovered completely (Table V).

TABLE V.—TIME COURSE OF RECOVERY IN FACIAL PALSY

Type	Total	Days to onset of recovery	Days to final recovery
Conduction block ..	173	10.05 ( $\pm 0.35$ )	46.3 ( $\pm 1.62$ )
Denervation ..	135	61.8 ( $\pm 3.24$ )	—

Figures in brackets indicate S.E. of Mean.

(5) *Relationship between the onset of movement and the degree of recovery.*—Although most of the CB group are well on the way to recovery, or cured, before many of the D group have begun to recover, there is considerable overlap between the two groups. In general, however, the earlier that movement begins to appear in patients in the D group, the greater is the degree of recovery. In Fig. 2 the mean recovery, expressed as a percentage of the power of the sound side (cf. Taverner, 1955), is plotted against the time of onset of the first sign of movement. When movement re-

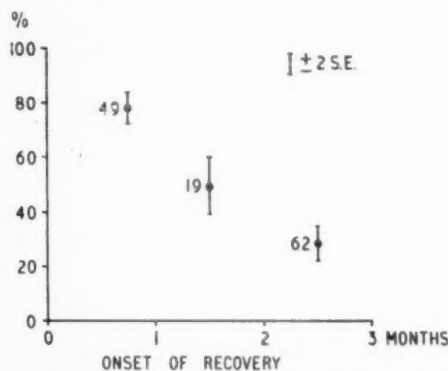


FIG. 2.—Relationship between time of onset of first signs of recovery and final degree of recovery. Ordinates: Final degree of recovery estimated as in Table VI. Abscissae: Time of onset of recovery. Figures show numbers in each group. Differences are statistically significant  $P < 0.01$ .

appears within one month of the onset of the paralysis the mean recovery is 78%, and between one or two months the mean recovery is 40%. No movement until the third month from the onset is followed by a mean recovery of only 28%. These differences are significant.

It can reasonably be concluded that the outcome in patients with denervation depends largely on its degree. Recovery by re-innervation can hardly occur in less than two months, so that the correlation of early onset of recovery with a high degree of return of power must mean that many of these patients have mixed lesions with only a proportion of their nerve fibres destroyed.

(6) *Eventual recovery after denervation.*—After denervation recovery of power begins to slow down after six months and there is rarely much improvement after nine months. Table VI shows

TABLE VI.—FINAL DEGREE OF RECOVERY OF MOVEMENT AFTER DENERVATION IN FACIAL PALSY

Degree	Number
0–30%	63 (38%)
31–70%	37 (23%)
71–97%	64 (39%)

164

Degree refers to the mean power of the frontalis and orbicularis oris muscles expressed as a percentage of the normal side.

the final assessment of power made on the 164 patients in this series who suffered denervation. About 40% show less than 30% of normal power and a further 40% have regained more than 70% of normal power.

(7) *Sequelae of denervation.*—It has already been established that all patients show some degree of associated movement and blink bursts after denervation (Taverner, 1955) and the same

result was found in this investigation. The proportion of other sequelæ is shown in Table VII. Only 43 (25%) of the D group were eventu-

TABLE VII.—SEQUELÆ OF DENERVATION IN FACIAL PALSY

No. at risk	Dissatisfied	Contracture	Excess tears	Crocodile tears
164	43 (25%)	113 (69%)	25 (15%)	15 (9%)

ally dissatisfied with their state, usually because of laceration or disfigurement by contracture. This is only about 1 in 10 of all those originally afflicted. Apart from associated movements, the commonest sequel of denervation was contracture, which was found in 113 (69%) of the patients. It was usually an asset because it tended to be prominent in patients with the least return of voluntary power and helped to produce facial symmetry at rest.

Lacrimation was the only other important sequel of denervation. In 25 patients (15%) this occurred in cold winds or when reading and seemed to be due to mechanical inefficiency of the lacrimal duct. In 15 (9%) of the patients the true crocodile tear phenomenon occurred, with tears streaming down the face while eating. Occasionally crocodile tearing may disappear again. The lacrimal duct becomes more efficient as power returns to the orbicularis oculi muscles and it seems to cope more effectively with the excess tears which can then be felt to run into the nose and throat during eating.

#### Discussion

The outcome of facial palsy depends on whether the facial nerve fibres suffer conduction block or whether some, many or all of them are destroyed, causing denervation, in some degree, of the facial muscles. The presence of denervation can be detected with considerable accuracy by electromyography and is found to occur in 40% of all cases. This figure is rather higher than in previous studies, perhaps because the criteria for its detection were rather stricter.

It is noteworthy that only about a quarter of the patients with denervation, and only about 1 in 10 of all patients, are seriously dissatisfied with their eventual state. This observation may be of importance in relation to treatment.

**Treatment.**—Our lack of success in treating facial palsy is evident from the number of different measures which have been advocated and which have been reviewed by Taverner (1955). The effect of treatment is always hard to estimate in a disorder with such a high spontaneous recovery rate as facial palsy. Controlled trials of treatment are uncommon but in the case of cortisone and physiotherapy I was unable to show any significant effect (Taverner, 1954, 1958).

**General management.**—Although we have no cure to offer these patients, they can be helped. The initial pain usually responds to analgesics and the patients then remain comfortable, in my experience, with daily self-massage, reassurance and explanation. It is important to see them frequently so that, by adequate electrical testing, they can be reassured about eventual recovery or warned about sequelæ if denervation should develop.

Mechanical support I find to be useless and even harmful to the skin. It is alleged to prevent over-stretching of the paralysed muscles but Henderson and Taverner (1949) have shown this to be of little practical importance. In older patients with denervation severe epiphora may lead to excess tearing which can sometimes be alleviated by supporting the lower lid with strapping.

Some patients with an exposed eyeball complain of constant, severe ocular pain which may be due to a punctate keratitis. If local applications fail to relieve it then a partial tarsorrhaphy is helpful. This need never be permanent, because the power to close the eye always returns eventually, no matter what the degree of denervation.

**Surgical treatment.**—Surgical treatment by decompression of the facial nerve in the stylo-mastoid (fallopian) canal has often been advocated for resistant cases (Ballance and Duel, 1932; Sander, 1934; Tickle, 1945; Cawthorne, 1952). There are no controlled studies available and theoretical consideration is therefore permissible. Decompression is based on the theory that the facial nerve swells in the bony canal and thus cuts off its own blood supply causing ischaemia. If this is mild conduction block ensues but if severe it causes destruction of the nerve and denervation of the muscle.

In addition to the theoretical objections previously adduced (Taverner, 1955), there is the important evidence of Sunderland and Cossar (1953). They showed that the facial nerve nowhere occupies more than half the cross-sectional area of the canal, the rest being filled by connective tissue and blood vessels.

It is fair, I think, to conclude that the case for surgery has not been established. It can never have a wide application because 6 out of every 10 patients recover completely in a short time. Denervation is not in itself a very serious matter and eventually only about a quarter of such patients are seriously disfigured or dissatisfied. Even if surgery is shown to be effective, we shall still have to find a way of discovering the one patient in every ten who is destined to do badly. Electromyography may not be the answer because

in animals it can be shown that the first electrical evidence of denervation appears more than forty-eight hours after a nerve has been severed (Taverner—unpublished observations). Even surgical treatment can hardly be retrospective.

In conclusion, then, I should like to designate facial palsy as an unsolved problem and to make a plea for properly controlled clinical trials of any new treatments.

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#### Electrical Changes Following Section of the Facial Nerve

In clinical electrodiagnosis, it is usually accepted that, after a peripheral nerve injury, a period of about two weeks must elapse before electrical evidence of nerve degeneration can be expected. However, Landau (1953) was able to detect changes before the end of the first week when he studied a small group of patients with complete nerve transections as the result of injury, the nerve fibres distal to the lesion becoming electrically inexcitable within four to six days. In 4 of Landau's 5 patients the motor nerve trunks in the limbs were involved but in the fifth patient the buccal branch of the facial nerve had been cut by glass, and in this case also complete loss of excitability was present after the fourth day.

In order to obtain more information about the time-course of degeneration in the facial nerve, we have studied the electrical reactions of the facial muscles in four patients with acoustic neuromata in each of whom the facial nerve was divided at operation. We have also studied 3 patients in whom the facial nerve was divided for the relief of hemi-facial spasm, and in this latter group we were able to combine electromyographic recording with electrical stimulation.

#### Observations on Patients with Acoustic Neuromata

We were anxious to study the effects of facial nerve section in patients without pre-existing damage to the nerve and although it is unusual for complete sparing of the facial nerve to occur in

cases of acoustic neuromata, it can be seen from Table I that the pre-operative state of our four patients approached this fairly closely.

TABLE I.—PATIENTS WITH ACOUSTIC NEUROMATA

Case	N.H. No.*	Age	Pre-operative state of facial musculature
M. D.	65874	60	Trace weakness lower face only.
A. C.	59515	55	Slight generalized weakness.
H. P.	67755	54	Weakness lower face only.
E. N.	60382	57	No weakness detected.

\*National Hospital number.

In each case total removal of the tumour was carried out by Mr. Wylie McKissock, the facial nerve being divided during the operation. Electrical testing was started on the second post-operative day and repeated daily until the end of the first week. Our stimulator was of the conventional type with a low impedance output, providing square wave pulses of 0.1, 1, 10 and 100 milliseconds duration, with a voltage range of up to 100 volts. In each case the upper fibres of orbicularis oculi were used for testing, the stimulating cathode being a small saline pad, 1 cm. in diameter, placed just above the eyebrow approximately 3 cm. from the mid-line. The anode was a large metal plate strapped to the arm.

At each daily examination the threshold voltage for a muscle response in orbicularis oculi was determined on both sides of the face for pulse durations of 0.1, 1, 10 and 100 milliseconds. Averaged results from the four subjects are plotted in Fig. 1, in which the mean threshold

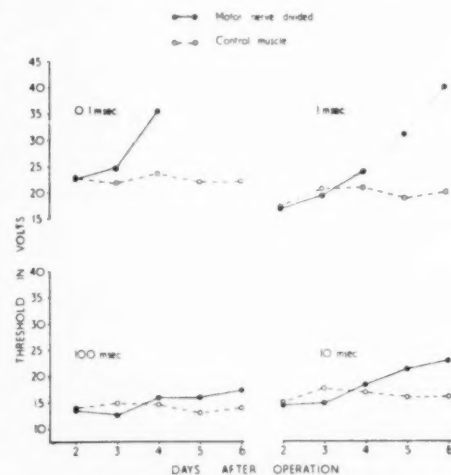


FIG. 1.—Electrical threshold of orbicularis oculi on successive days after section of facial nerve. Mean voltage required to excite affected and control muscles in four subjects is shown for pulse durations of 0.1, 1, 10 and 100 milliseconds. (For further explanation see text.)

voltages on successive days are shown separately for the four stimulating pulses used. On the unaffected side of the face there was little change from day to day but for the denervated muscles the threshold voltage for short duration pulses rose sharply during the week. With the 0.1 millisecond stimulus there was no appreciable difference between the two sides of the face on the second post-operative day, but on the third day a slight rise in mean threshold occurred on the denervated side. On the fourth day, a still higher voltage was required to stimulate the affected muscles, and after this day it was not possible to obtain a twitch with this stimulus, even when using the highest voltage tolerated by the patients. The 1 millisecond stimulus revealed only a small difference in threshold between the muscles of the two sides on the fourth post-operative day, but on the fifth day there was a sharp rise on the affected side. In Fig. 1 the points for the fifth and sixth days have been joined to the rest of the curve by a dotted line to indicate that a response was not obtained in all four patients; on the fifth day the threshold voltage could be reached in only two patients and on the sixth day in only one. The stimulus intensity necessary to elicit a contraction was not reached in the others as the higher voltage shocks were excessively painful and the full output of the stimulator could not be used. The dotted part of the curve in Fig. 1 is, therefore, less steep than the true curve would have been if values for all four patients had been obtained (e.g. by stimulation under anaesthesia).

In contrast to the results with short duration pulses, the mean threshold for the 10 millisecond stimulus rose only slightly on the denervated side and the threshold for pulses of 100 milliseconds duration (corresponding to the rheobase in a full strength-duration curve) showed little change.

#### *Observations on Patients with Hemi-facial Spasm*

3 patients were studied in whom the facial nerve had been divided for relief of distressing hemi-facial spasm.

*Case I.*—Mr. E. L., aged 61 (N.H. No. 65174), first noticed involuntary twitching and spasm of the left facial muscles in 1949. In spite of four attempts at alcohol injection of peripheral branches of the facial nerve, the involuntary movements gradually increased. By the time of the patient's admission to the National Hospital in May 1956, attacks of twitching of the left face were very frequent; voluntary contraction of the left facial muscles was noticed to be slightly weaker than on the right. In May 1956 the left facial nerve was explored within the facial canal by Mr. Cawthorne and divided with scissors 4 mm. above the stylomastoid foramen. The cut ends of the nerve were placed in close apposition and covered with

amniotic membrane. Electrical testing was carried out immediately before operation and then daily for nine days.

*Case II.*—Mrs. E. J., aged 68 (N.H. No. 45686), had suffered from gradually increasing twitching and spasm of the right facial muscles since 1951, for which the facial nerve was divided within the temporal bone by Mr. Cawthorne in March 1956. This produced only transient benefit and in March 1957 the facial nerve was re-explored and a segment of nerve 1 cm. long removed from the region of the previous section. Electrical testing was carried out immediately before the second operation and then daily for six days.

*Case III.*—Mrs. E. B., aged 51 (N.H. No. 81878), first noticed the gradual onset of twitching of the right face in 1957, which slowly increased during the following year. On admission to the National Hospital in October 1958, frequent and painful involuntary spasms of the right facial muscles were present, voluntary contraction of the affected muscles being slightly but definitely weaker than on the unaffected side. In October 1958 the right facial nerve was divided within the right temporal bone by Mr. Cawthorne, the operative procedure being similar to that described for Case I. Electrical testing was carried out immediately before operation and then daily from the second to the eighth post-operative day.

In all 3 patients a standard electrical examination was carried out pre-operatively and then daily until the nerve became unexcitable. At each examination, the facial nerve trunk was stimulated percutaneously just in front of the ear, the stimulus being a brief condenser discharge with a time constant of 70 microseconds. A saline pad 1 cm. in diameter was used as the stimulating cathode and the anode was a large metal plate strapped to the neck or to the arm. For recording, a small co-axial needle was inserted into the upper fibres of orbicularis oculi immediately above the eyebrow and about 3 cm. from the mid-line, the muscle action potentials being amplified in the usual way and displayed on a cathode-ray oscilloscope. With the stimulus locked to the time base of the oscilloscope it was therefore possible to display the muscle response to a single brief shock delivered to the facial nerve. The distance between the stimulating cathode and recording needle varied from 9 to 11 cm. in different patients and stimulus intensity, although limited by the tolerance of the patient, was always greater than that necessary to produce a maximal response from a normal nerve.

The results in the 3 patients are shown in Table II from which it can be seen that although the visible muscle twitch in response to nerve stimulation disappeared within three or four days, an electrical response persisted in each case for a further forty-eight or seventy-two hours. By this time, however, the electrical response was much

TABLE II.—PERSISTENCE OF MUSCLE RESPONSE TO NERVE STIMULATION AFTER OPERATION

Case	Visible twitch survives	Electrical response survives
I.—E. L.	4 days	7 days
II.—E. J.	2 days	4 days
III.—E. B.	4 days	6 days

reduced in size, indicating that very few motor units in the region of the recording needle could still be activated. Specimen records from Case III are shown in Fig. 2; it can be seen that there was no real change in the evoked muscle action potential on the third post-operative day, but that obvious diminution in the response was present after that time, the response finally disappearing altogether on the seventh day. On simple inspection of the face, orbicularis oculi in this patient appeared to become inexcitable on the fourth day, which illustrates the point already

made, that a small electrical response may be evoked from a muscle which appears clinically to be totally inactive.

Table III shows the latency of the muscle response in each patient both before operation and on the last day on which a response was obtained and it can be seen that little if any increase in latency occurred during this time, suggesting that impulses were propagated with an approximately

TABLE III.—LATENCY OF MUSCLE RESPONSE AFTER NERVE SECTION

Case	Pre-operative		Post-operative	
	Conduction distance (cm.)	Latency in msec.	Conduction distance (cm.)	Latency in msec.
I.—E. L.	10.5	4.0	10	5.1
II.—E. J.	10	4.0	10	4.8
III.—E. B.	11	4.2	10.5	3.5

normal velocity in surviving motor fibres for as long as any conduction was still possible. This is a finding of some interest as we know that during regeneration the situation is very different, conduction velocity being extremely slow. For comparison with Table III, latency measurements are shown in Table IV for regenerating nerve fibres after facial paralysis due to a variety of causes.

TABLE IV.—NERVE CONDUCTION DURING RECOVERY FROM FACIAL PARALYSIS

Case	Cause of paralysis	Time after onset (months)	Conduction distance (cm.)	Latency of muscle response (msec)
E. B.	Nerve section	6	10	20.2
M. W.	Herpes zoster	7	11	12.0
E. H.	Head injury	8	9	8.0
F. W.	Bell's palsy	5	9	8.6

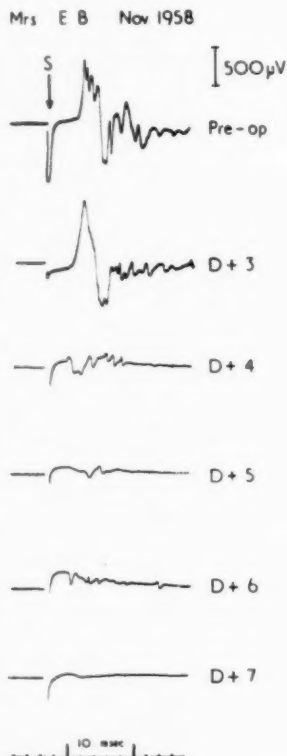


FIG. 2.—Tracings from Case III to show muscle response to nerve stimulation before and on successive days after nerve section. The stimulus (S) is shown by artifact in each trace and is followed by muscle action potentials up to the sixth post-operative day (D+6) but not after this time.



FIG. 3.—Tracings from Case III six months after nerve section. A small delayed muscle response to facial nerve stimulation is seen on the affected right side which may be compared with the normal response obtained on the left. The stimulus (S) is shown by artifact in each trace.

In each case the stimulating and recording electrodes were in the standard position already described, so that the conduction times are directly comparable with those obtained during degeneration.

Slowing of conduction during regeneration was particularly marked in Mrs. E. B. (Case III), and Fig. 3 shows records taken from this patient six months after operation. Tracings from the normal and the affected sides are mounted together to illustrate the difference in conduction rate over approximately the same length of nerve.

### Conclusions

Our results clearly confirm Landau's observations on the effects of nerve section. In the facial nerve, electrical evidence of degeneration can be expected on the fourth day after section, the changes becoming increasingly obvious during the next forty-eight hours. In patients with Bell's palsy the time-course of degeneration is certainly not always as rapid as this, and we accept that re-examination up to two weeks may be necessary in some cases before one can be sure that degeneration of the distal part of the nerve is not going to occur. Leading directly from this, it would be interesting to know whether those cases of Bell's palsy which degenerate slowly show a better long-term result than those in which the rapidity of degeneration approaches that seen after nerve section.

In assessing patients with Bell's palsy, it is clearly important to know whether degeneration is partial or complete, and our results suggest that electromyography may reveal surviving motor unit responses to nerve stimulation at a time when no twitch can be seen in the muscles concerned. In such a case nerve stimulation without electromyographic recording might give rise to an unnecessarily gloomy view of the situation.

Slowing of nerve conduction during regeneration is a well-recognized phenomenon in the motor nerves of the limbs (Hodes *et al.*, 1948) but, as far as we are aware, it has not been described previously in the face. The few examples which we have encountered suggest that this phenomenon would repay further study.

*Acknowledgments.*—We are indebted to Mr. Terence Cawthorne and Mr. Wylie McKissock for permission to investigate patients under their care. We particularly wish to thank Mr. Cawthorne for his encouragement and advice.

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### Facial Palsies and their Treatment

In 1814, Sir Charles Bell cut the facial nerve of a monkey and found that a facial paralysis on the same side resulted from this section. He had proved then that this nerve was responsible for facial movements. More than one hundred years later, Sir Charles Ballance and Arthur Duell suggested exposure of the nerve at the site of the lesion for relief of persisting peripheral facial paralysis. It had been Dr. Sullivan's good fortune to have been associated with them in that original work.

During development, the facial nerve is enveloped in cartilage, pushed in various directions by the developing inner and middle ear segments; the pushing accounts for the devious course of the facial nerve. The nerve then becomes frozen in bone and supplies the derivatives of the second or hyoid arch. As with other motor and sensory nerves the fibrils are covered by myelin and nourished by the Schwann cell of the neurilemma sheath. Perineurium covers the endoneurium and epineurium shrouds of the bundles to make a nerve as we see it in the gross. The blood supply, lymph and venous drainage are remarkable since this nerve passes through more bone than any other. The facial branch of the internal auditory artery supplies the petrous portion, the middle meningeal supplies the geniculate and tympanic portions and the stylomastoid artery supplies the vertical segment.

The anatomy of the nerve is well described in all texts; one important point is that the position of the pyramidal segment between the tympanic and vertical parts depends on the pneumatization of the bone. Even in a radical mastoid cavity with complete exposure of the tympanic segment, the bend must be exposed carefully. Rather than expose the nerve on its anterior or middle ear side, it should be exposed posteriorly to protect the blood supply which lies anterolateral to the nerve. It should be remembered that the facial nerve consists of three components: (1) Motor to the facial musculature, (2) parasympathetic to the salivary glands (except the parotid) and (3) sensory from the sphenopalatine and chorda tympani nerves.

*Electrical reactions in diagnosis.*—Normal responses to the faradic and galvanic currents indicate normal nerve function, but they are merely aids to diagnosis. Absence of a faradic reaction (interrupted current) suggests early wallerian degeneration. Loss of the galvanic reaction (continuous current) indicates muscle atrophy. When there is not any contraction present with either current, the reaction of

degeneration has occurred. Electromyography is more accurate; it is slightly more painful, but may tell us that early return of function can be expected. Fibrillation on the tracings indicates a degenerative lesion and may show up about three weeks after the onset of paralysis (reaction of degeneration). While none of these tests is foolproof, repeated tests aid in observation of the progress of the patient.

*Central lesions producing facial paralysis and their treatment.*—Any surgical treatment of facial palsy resulting from a central lesion is aimed at cosmetic improvement only. Most frequently a lesion of the central nervous system causing facial paralysis is associated with a hemiplegia. Other causes, such as tumours, disseminated sclerosis and so on, make the treatment of facial paralysis a less important factor than the care of the general disability. The lower face is paralysed since there is bilateral representation of the frontalis and orbicularis oculi regions. Cerebellar pontine angle tumours and neurofibromata of the VIII nerve rarely cause facial paralysis unless they have attained a considerable size. An excellent paper by Harrison (1954) describes the Ramsay Hunt syndrome and states that only 6 of 12 patients studied obtained return of function. Cortisone is the only new treatment suggested for this syndrome.

The treatment of these patients depends on the individual ideas of the particular physician treating the case. Some suggest hypoglossal anastomosis, others facial slings with cosmetic repair to the soft tissues. An intra-oral prosthetic appliance is useful for all types of facial paralyses. This appliance consists of a plastic wire attached to the molar teeth or dental plate to hold the mouth in the desired position. It is fitted by an oral surgeon. The treatment, therefore, is an individual problem depending on age, prognosis and complicating factors.

#### PERIPHERAL FACIAL PARALYSIS

*Bell's palsy.*—We advise our patients to wait for six to eight weeks before considering decompression and neurolysis. The patients treated by these methods are those who show no facial movement after this waiting period or those in whom recovery is incomplete.

Neurologists in many centres continue to teach watchful expectancy and when a patient is finally referred it may be too late. Some interesting points and fallacies in the diagnosis and treatment of this malady will be mentioned. We feel the only reliable test of the extent of the lesion is in the presence or absence of taste in the anterior two-thirds of the tongue on the affected side.

Tests for stapedial muscle power are useless since the tensor tympani muscle supplied by the trigeminal nerve evidently relieves the disability. Decompression of the tympanic segment is unnecessary in this type of Bell's palsy; interference with the incus as well as a modified radical operation is unjustified. Middle-ear disease involving the attic or aditus necessitates an exploratory modified procedure; it could be diagnosed from the history and roentgenographic examination prior to operation.

The endaural approach is satisfactory for those familiar with the mastoid from this view. The postauricular approach is advantageous because the stylomastoid foramen can be enlarged much more easily; this is the most important part of the procedure in decompression. Rather than expose the middle ear anterior to the fossa incudis, we use suction irrigation, magnification and a large finishing burr just below the fossa incudis; profuse bleeding is the first indication of proximity to the nerve. The vertical segment of the nerve is exposed by uncovering the remaining thin plate of bone with a fenestration curette. Again, the important point is to expose the stylomastoid foramen adequately. The microscope is then used when the surgeon slits the epineurium down its posterior aspect; as this is done the compressed blood vessels fill with blood and the nerve bulges outward, that is, if fibrosis has not occurred.

The nerve is covered with Gelfoam and the incision closed without drainage. Recovery may begin the following day or it may take months. Galvanic stimulation three times a week can be prescribed in the sluggish case. A patient who has had a Bell's palsy for six months without recovery rarely attains normal function even after decompression. We must not forget that 85% of the patients with Bell's palsy recover without surgical treatment; however, we are interested in the 15% that must receive help.

*Operative injury.*—A small fragment of bone which pierces the sheath can be removed gently; the nerve need not be decompressed if oedema is slight. However, packing must not be placed over this area. Decompression of the nerve does not, in itself, produce facial paralysis if carried out carefully on a normal nerve. If paralysis occurs within twenty-four hours or is present immediately after the operation, the nerve should be decompressed as soon as possible. Of course, Novocain injection can produce a harmless twenty-four hour paresis. Secondary oedema is the cause of paralysis after the third or fourth day and conservative treatment with cortisone and antibiotic cover is sufficient; however, all packing should be removed immediately at the onset of

the paralysis. Any injury to the nerve during stapes mobilization will have to be assessed by the surgeon. An immediate facial paralysis following a fenestration operation is indeed a problem. This patient should be taken back to the operating room and the site of injury determined. Usually the flap at the level of the chorda tympani nerve can be incised without disturbing the fenestra and then a routine decompression is carried out.

The possibility of an aberrant course of the facial nerve must be remembered during the surgical management of congenital atresia. When the usual landmarks are absent or undeveloped, identification of the nerve is often difficult. One adult with congenital atresia had a 30 mm. gap of the nerve. This was caused by the surgeon approaching the antrum at the usual point when the nerve was covered by a thin plate of bone just under the skin in its vertical segment. This surgical gap was bridged with a graft.

Sooner or later myringoplasty procedures will take their toll due to over-zealous packing over the graft, since the facial nerve has a very thin bony covering in the tympanic segment or the bony covering may be defective. When a piece of nerve has been accidentally removed with a curette or burr during a mastoid operation, the nerve should be decompressed by the surgeon, the nerve sheath slit and the rough edges trimmed to a right angle. End-to-end anastomosis is then preferable, if possible. A graft, when necessary, is removed from the upper lateral cutaneous nerve of the thigh; the great auricular nerve may be used. The latter closely parallels the external jugular vein posteriorly and crosses the sternomastoid muscle superficially just above its midpoint. The nerve graft is trimmed to the exact length desired and handled without excess trauma. It is placed in position and held by plasma glue; the cavity is then covered by a further thick layer of glue and the incision closed without drainage. Antibiotics are prescribed in every case.

End-to-end union must be done without tension at the site. If the nerve has been cut at the stylo-mastoid foramen and time allowed to elapse, the formation of scar tissue makes the operation difficult since the peripheral segment is often very firmly embedded in scar and impossible to identify. A faradic current stimulator used at the time of operation is helpful in identifying the peripheral segment.

Recovery after grafting or end-to-end union is never wholly satisfactory if the lesion has been present for longer than twelve months. Associated movements occur and emotional response is seldom if ever present. The first sign of recovery is usually at the corner of the mouth and does not occur for at least six months after the graft. Recovery may take more than eighteen months

and the patient should be told this before the operation. Continued galvanic overstimulation may produce tics. A mouth hook and a tarsorraphy are also advised.

Martin and Helsper (1957) have cited several instances of spontaneous recovery of the facial muscles after removal of a large segment of facial nerve trunk and branches during parotid surgery for carcinoma. This recovery occurred six months or longer after operation and they feel it was due to synapse connexions of the trigeminal nerve with the facial nerve. We have noted early movement at the corner of the mouth which we felt was due to buccinator contraction. It is difficult to argue against this interesting theory; however, we have treated patients using grafts from 6 to 20 mm. long and obtained complete functional recovery six months after the operation with a normal emotional response. We also have removed sections of grafts in animals in which neurofibrils, present in fairly large numbers, pass *through* the graft to prove that nerve grafts do function. The trigeminal nerve may also assist in recovery.

This type of nerve surgery does emphasize the urgency of quick repair in order to obtain good results.

*Chronic suppurative otitis media.*—Facial paralysis is an uncommon complication of chronic suppurative otitis media. When it does appear, the nerve should be decompressed as soon as possible, and a modified or radical mastoidectomy done at the same time. Granulations or cholesteatoma frequently expose the nerve in its tympanic segment and this is found at the time of operation on patients with no history of facial weakness; these patients do not require decompression. If decompression is carefully done on a normal facial nerve, no paralysis occurs. Decompression is a harmless procedure if it is performed under microscopic surgical vision.

*Skull fracture.*—Neurologists are sceptical as to the benefit of decompression in cases of fracture involving the nerve. If they could observe a shearing fracture of the vertical segment with compression of the nerve they might agree that we are correct when we teach that two months is long enough to wait before decompression. Vestibular or cochlear damage suggests a fracture through the petrous bone, and exploration of the nerve in this area is indeed difficult. Petrous exploration seldom results in recovery after operation. Frontal and occipital fractures predispose to petrous fractures in an anterior-posterior direction whereas temporal fractures usually involve the tympanic and vertical segment of the nerve. Variations in these fractures make radiologic

diagnosis difficult. The ossicles may often be dislocated, as we have noted in some middle-ear operations on patients with a history of head injury. Plastic repair with fascial supports is suggested if recovery has not occurred within two years in a patient whose paralysis was inoperable.

*Wounds.*—A common site for injury is near the stylo-mastoid foramen; we suggest immediate repair by end-to-end anastomosis if it is practical in the particular case. If the injury is close to the mouth, the branches are really too small to identify and repair; watchful expectancy is the rule for treating this type of case. The injudicious removal of foreign bodies in the ear canal may be followed by facial paralysis due to injury to the tympanic segment.

*New growths.*—Most surgeons agree that if a new growth involves the facial nerve excision of the nerve with the tumour is the only accepted procedure. Eradication of the tumour is more important than immediate plastic repair. We have recently seen a neurofibroma of the descending portion of the nerve which was removed in part leaving facial function only temporarily impaired (Kettel, 1959).

*Parotid surgery.*—The first requisite in this type of operation, regardless of the condition, is to identify the nerve at the styloid process and trace it forward into the gland. Removal of the gland in chronic parotitis or with mixed tumours or carcinoma can be performed safely and the nerve preserved. If a small portion of the nerve is removed with the tumour, end-to-end union should be done; if the main trunk has to be

removed with the growth, we suggest continued observation of the area without nerve grafting. In this regard we agree with Martin and Helsper. If a mixed tumour has been removed with part of the nerve, a graft could be used as suggested by Conley (1955) who prefers to use the great auricular nerve and buries the branched graft into facial muscles. Fusion of the eyelids is done at the time of the operation if prolonged facial paralysis is expected.

*Hemi-facial spasm.*—This condition is the reciprocal of Bell's palsy. It is caused by some irritation of the facial nerve in its course and produces involuntary twitching of the face as a subjective complaint. The treatment has included decompression, partial section, complete section, and removal of a segment with reversal of the graft and replacement. All methods are about 50% successful.

In all types of surgical procedures on the ear, the nerve should be immediately identified and made a landmark. Surgery should try to remove the cause of the paralysis as soon as it appears that all medical treatment has failed. Mass movements occur with over-stimulation or may result from delayed surgical treatment. Not even a well-trained otologic surgeon can afford to become careless in his treatment of the facial nerve.

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 MARTIN, H., and HELSPER, J. T. (1957) *Ann. Surg.*, **146**, 715.

*Meeting*  
 July 17, 1959

#### LARYNGOLOGICAL SESSION

Chairman—R. L. FLETT, F.R.C.S.  
 (President of the Section of Laryngology)

DR. HANS VON LEDEN (Chicago) showed films demonstrating some physiological points with regard to the larynx and commented thereon.

Following the films a Discussion was held on *Laryngeal Physiology* in which the following speakers took part—SIR VICTOR NEGUS, MR.

MAXWELL P. ELLIS, MR. F. C. W. CAPPS, and MR. R. L. FLETT.

DR. HANS VON LEDEN replied to the Discussion.

The meeting will be reported in the *Journal of Laryngology*.

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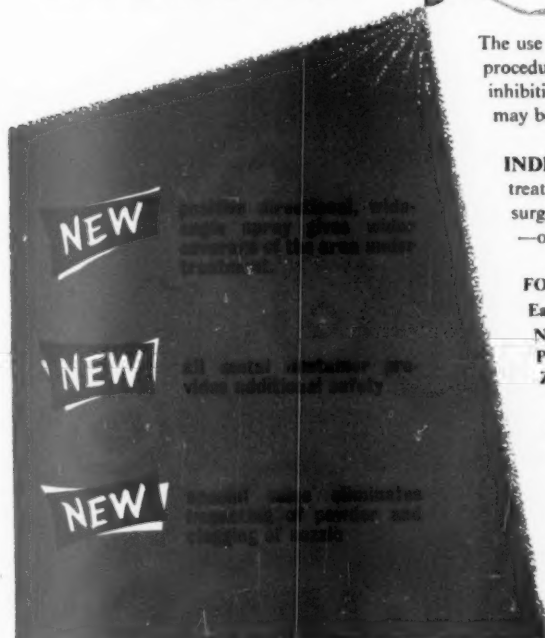
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## Section of Radiology

President—B. W. WINDEYER, M.R.C.P., F.R.C.S., F.F.R.

Meeting  
February 20, 1959

### SYMPOSIUM ON THE CHANGING PATTERN OF OROPHARYNGEAL CANCER [Abstract]

THE Symposium was opened by **Dr. Jens Nielsen** (Copenhagen).

**Sir Stanford Cade** (London) dealt with changes in the incidence, diagnosis and treatment of oral cancer. He noted a remarkable fall in incidence since 1911 to under one-third of the rate then obtaining. This fall has affected men only—a slight rise in the incidence of mouth cancer in women has altered the ratio from 10 to 1 in 1925–29 to 2 to 1 in the period 1951–55.

Diagnosis has been simplified by the elimination almost completely of such differential lesions as gumma, tuberculosis and actinomycosis. Recognition of precancerous conditions such as leukoplakia and erythroplasia has led to earlier treatment.

Radiotherapy remains the first line of treatment and the speaker's choice still lay with radium implant. Other radioactive sources have their place. Dosage tended to be a little higher. Supervoltage therapy has marked a big step forward in the ability to deliver a high dose with minimal disturbance to the patient.

Advance in the surgery of oral cancer owes much to modern anaesthesia. Extensive eradication and reconstruction of tissue is possible in a deliberate and planned manner. This, in conjunction with radiotherapy, has greatly improved the outlook in many of the more extensive lesions.

**Dr. Ralston Paterson** (Manchester) also noted the lowered incidence of oral cancer in men. This was not so for women, but the cure ratio for them was decidedly higher (ten-year survival:

male 28%, female 45%). The incidence of pharynx-larynx cancer had slightly increased but this was small in relation to the increase of cancer in other sites.

Methods of treatment were changing in the direction of introducing supervoltage irradiation especially for the less accessible cancer. Radium still proved the most satisfactory in more than half the cases. In early laryngeal cancer the Finzi-Harmer fenestration implant still had a high degree of reliability while the cobalt-loaded bougie plus external irradiation for the post-cricoid lesion was still in his opinion the best treatment for appropriate cases.

The overall results in Manchester for oral cancer for the three test periods 1934–39, 1940–45, 1946–52 showed (five-year survival) 39%, 49% and 52% respectively. There was a real improvement, but less in the later than in the earlier period. The corresponding figures for pharynx-larynx cancer were 23%, 26% and 47%. Here recent improvement was the more striking.

On comparing the results of implant technique with beam-directed X-rays in a series of similar faucal cancers, it appeared that, while the results differed little in early stages of growth, in the late cases there was a decided bias of advantage towards the X-ray technique.

The development of supervoltage combined with improvement in techniques and accuracy gave promise of further progress.

**Mr. C. P. Wilson** (London) also took part in the discussion.

Meeting  
March 20, 1959

**Dr. F. G. M. Ross** showed a film entitled *Cineradiographic Demonstration of the Bile and Pancreatic Ducts*.

Papers were read as follows:

**Non-osteogenic Fibroma of Bone.**—**Dr. W. M. Purcell** and **Dr. F. Mulcahy**. (To be published in *Clinical Radiology, Journal of the Faculty of Radiologists*, 1960, 11.)

**The Value of Arteriography in the Diagnosis of Bone Tumours.**—**Dr. B. Strickland**. (See *British Journal of Radiology*, 1959, 32, 705.)

**Benign Lesions Mimicking Malignant Bone Tumours.**—**Dr. E. Samuel**.

Meeting  
April 17, 1959

## Chordoma

### PRESIDENT'S ADDRESS

By B. W. WINDEYER, M.R.C.P., F.R.C.S., F.F.R.

London

CHORDOMA is a relatively rare tumour which arises from the remnants of the notochord.

#### *The Notochord*

The notochord in the embryo extends from the speno-occipital junction to the coccyx. It has been shown that in the human, at its upper end, it approaches the inner surface of the sphenoid and may lie in close proximity to the dura. More caudally it comes closer to the pharyngeal surface of the occipital bone. In both these situations remnants of chordal tissue have been observed on the surface of the bone. The notochord later becomes divided into segments with the development of the vertebral column, and disappears as an entity. Within the vertebral bodies occasional vestigial remnants have been observed and in the intervertebral discs the notochord is represented by the nucleus pulposus. I am indebted to Professor E. W. Walls for these illustrations of the notochord in a 21 mm. (seven

weeks) human embryo cut in the sagittal plane (Figs. 1A, B).

Luschka in 1857 was the first to discover small jelly-like protrusions into the skull from the region of the clivus of Blumenbach and these were described by Virchow in 1857. He considered that they were cartilaginous in origin and named them "ecchondrosis physaliphora", believing that the vacuolated mucus-containing cells were degenerated cartilage cells.

Müller in 1858, after a study of the notochord in the foetus and of notochordal rests in man and animals, was the first to put forward the view that these excrescences were derived from the notochord. His view was not upheld and the opinion of Virchow, as to their cartilaginous origin, was generally accepted until Ribbert in 1895 finally established their origin from the notochord, and that they were in fact "ecchord-

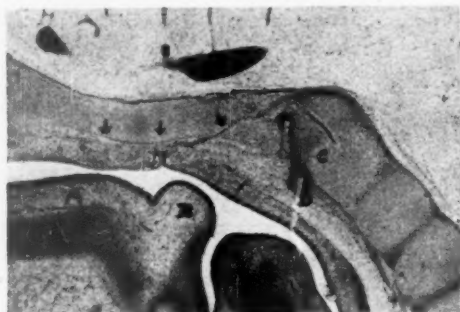


FIG. 1A.

FIG. 1.—Sections of 21 mm. (seven weeks) human embryo in sagittal plane.

FIG. 1A.—Cephalic end showing notochord (arrowed) extending through odontoid peg and curving towards the pharyngeal surface of the occipital bone and then up towards the dural surface of the sphenoid. Its termination is caudal to the developing pituitary. A, Tongue. B, Epiglottis. C, Axis. D, Anterior arch of atlas.

FIG. 1B.—Caudal end of foetus showing the remains of the notochord in the developing vertebral column. Segmentation is commencing with the development of bulges to form the nucleus pulposus of the intervertebral discs.

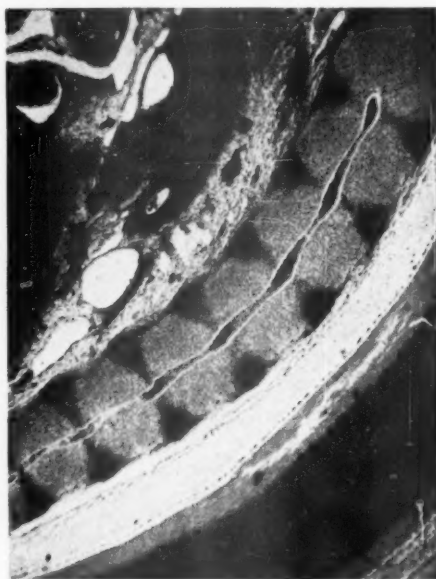


FIG. 1B.

oses". He was the first to apply the term "chordoma". He conducted experiments on rabbits, piercing the intervertebral discs and allowing protrusion of the nucleus pulposus. Eventually these herniations enlarged with an appearance in all ways resembling that of a chordoma.

Echordoses, or heterotopic notochordal remnants in the speno-occipital region, are uncommon, but are occasionally found if carefully sought at autopsy. Ribbert found them in 2% of examinations. Stewart and Morin (1926) found 4 in 350 autopsies, and Willis (1953) found 5 in over 1,000 examinations in which he had looked for them. They are quiescent, symptomless protrusions consisting of irregular vacuolated cells in a mucoid matrix. Similar heterotopic notochordal remnants have been described in the coccygeal region. It seems probable that they may in some cases be the starting point of a chordoma.

Several cases of chordoma, a progressive tumour causing symptoms, were described in the region of the clivus in the first decade of this century, and sacrococcygeal chordoma was first recognized in 1910 (Alezaïs and Peyron, 1914; Berard *et al.*, 1922; Feldmann, 1910). In 1922, Stewart described the first case in Britain, a sacrococcygeal growth, when there were only 26 cases in the literature. Since then there have been increasing numbers of cases reported (Alexander and Struthers, 1926). Mabrey (1935) reviewed the literature up to that date and collected reports of 150 cases. Harvey and Dawson (1941) reviewed 240 cases, and in 1944 Faust *et al.* brought the total up to 252. Dahlin and MacCarty (1952) reported 59 cases from the Mayo Clinic and in later years there have been smaller series and individual cases. Crawford (1958) described the staining reactions of these tumours and added a further 6 cases. The total number described up to the present must be more than 350.

This present study is based on observations on 29 cases which have not previously been reported. 4 of them were under the care of Sir Stanford Cade at the Westminster Hospital, and I am indebted to him for placing his cases at my disposal. The remainder have been in the Middlesex and Mount Vernon Hospitals, where I have had the opportunity of studying them and of treating the majority of them.

The cases of chordoma which have been described arise most frequently at the upper and lower extremities of the vertebral column, the portions which are the last to develop. 90% are

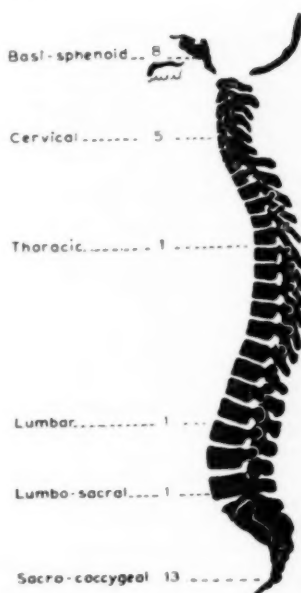


FIG. 2.—Sites of origin of chordomata in author's series.

in the speno-occipital and sacrococcygeal regions, but they also occur in the cervical, thoracic and lumbar regions (Fig. 2, Tables I and II).

TABLE I.—SITES OF ORIGIN IN AUTHOR'S SERIES

Spheno-occipital	8
Cervical spine	5
Thoracic spine	1
Lumbar spine	1
Lumbosacral spine	1
Sacro-coccygeal	13
The distribution is similar to that in other series.	

TABLE II.—SITES OF ORIGIN IN OTHER SERIES

	Present series	Dahlin and MacCarty (1952)	Harvey and Dawson (1941)	Mabrey (1935)
Sacro-coccygeal	13	32	122	87
Spheno-occipital	8	15	88	47
Vertebral	8	12	30	14
Others	—	—	—	2
	29	59	240	150

#### Age and Sex

Chordoma has been reported in any age group from infancy to the very old. They are more frequent in later life and those arising in the sacrococcygeal region are usually in an older age

group than those in the region of the clivus or elsewhere in the spine.

In the present series the youngest was 8 and the oldest 66. All but 3 were over 30 and more than half were over 40. The average age of patients with tumours in the sacrococcygeal region was 49 years, as against 36 years for the remainder. In the reviews of Harvey and Dawson, of Mabrey and of Dahlin and MacCarty, there was a preponderance of males over females in the proportion of about 2 to 1. In this series, however, the sex incidence is nearly equal. 15 were male and 14 female.

It has been pointed out that in the sacrococcygeal tumours there is a frequent history of trauma preceding the development of the tumour. In 4 of the cases which I have studied there was such a history of a severe fall followed by persistent pain, leading on to recognition of a tumour. 3 of them were sacrococcygeal and the other one was in the lumbar region. The observation of a history of trauma is an interesting one, but a correlation of cause and effect must be treated with some reserve. There is always a tendency in any case of tumour formation for the patient to remember some particular blow or fall preceding the discovery of the growth, and in sacrococcygeal chordomas there is the possibility that the presence of the neoplasm may have produced some weakness of the legs and been instrumental in the fall. As Cappell (1928) has pointed out, the experiments of Ribbert are, however, suggestive that trauma may play a part in the development of these tumours.

#### Pathology

The typical chordoma is a slowly growing, locally invasive tumour which causes irregular destruction of bone and extends into the soft tissues, tending to compress and push them aside and erode them rather than to infiltrate them. The bone at the site of origin may show extensive absorption and the periosteum and cancellous bone at the edges of the defect, where the tumour has broken through into soft tissue, are expanded and pushed out over the soft tissue mass.

**Macroscopic appearance** (Fig. 3).—On cut section the tumour has usually a variegated appearance. Much of it is solid, of a gelatinous consistency, and there may be large cystic areas filled with a semi-fluid mucinous material.

The tumour may be divided into lobules by bands of fibrous tissue and it may appear to have a fibrous capsule around it. In some parts there may be areas of necrosis and others may be

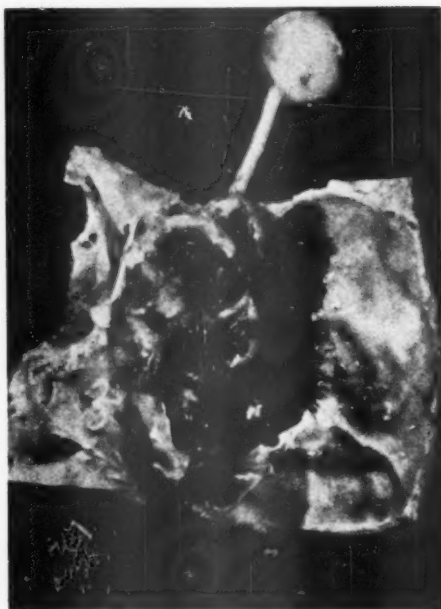


FIG. 3 (Case 1).—Macroscopic appearance of a chordoma.

deeply pigmented from old hæmorrhages, and in some cases there are bone fragments apparently carried out with the advancing tumour from the vertebra of origin. In one of the cases in this series there was considerable calcification in the tumour.

**Histology** (Fig. 4).—The histological appearances of chordoma have been described in detail in several publications. They show a picture in which there is great variation. The cells may be packed together in solid irregular groups separated by connective tissue or by a mucinous matrix. They may be in cords or trabeculae and in the case of Alezais and Peyron (1914) there was the presence of regular cavities lined with cuboidal cells.

There is great variation in the size of the cells. In the youngest part of the tumour there are small polyhedral cells, and in the older parts the cells are larger with vacuolated cytoplasm and intercellular vacuolation. These were described as physaliphorous cells by Virchow, and are the characteristic feature of chordoma. The blown-up physaliphorous cells may gradually lose their cell outline and in parts there may be the appearance of a vacuolated syncytium, with few cells swimming in a sea of mucus. The vacuolated

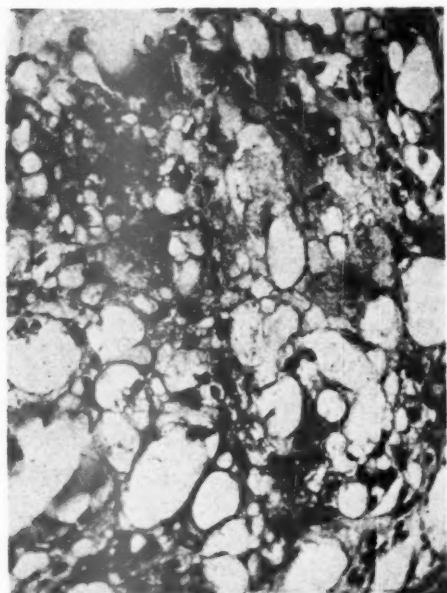


FIG. 4.—Histological appearance.

cells may have a signet ring appearance and vacuoles in the nucleus have been described. In one of Willis's cases there were many giant cells, some of huge size, and both Cappell (1928) and Willis (1953) have described a distinct hyaline sheath delimiting the chordoma from the surrounding tissues. Cappell has also pointed out that the great variation in histological appearance of chordoma is consistent with the histological appearances of the notochord in its various stages of development. In some parts of a chordoma a definitely spindle cell appearance has been described, closely resembling fibrosarcoma. In some, the mucinous matrix and the vacuolated cells may be difficult to distinguish from cartilage and there may be difficulty in differentiating chordoma from chondrosarcoma, a differentiation which Crawford (1958) considers can be made with special staining methods. Lichtenstein (1952) draws attention to the possibility of a false diagnosis of colloid carcinoma of the rectum being made in sacrococcygeal chordomas.

Stewart (1922) considered that chordoma could only be diagnosed with certainty if the characteristic vacuolation and mucin production are present in at least a portion of the growth.

#### *Metastases in Chordomas*

The usual course of a chordoma is to increase gradually but slowly, and there may be a history of discomfort or pain extending over some years before a diagnosis is made. In some cases, however, the progress may be much more rapid and there may be a history of only a few months before a tumour of considerable size is found, and in many of the cases described the rate of growth has increased considerably in the later stages of the patient's illness. Chordoma, particularly in the sacrococcygeal region, may develop into an enormous tumour weighing many pounds. The eventual outcome in the majority of cases has been death, due to local extension of the tumour mass causing interference with function by reason of its bulk, or by involvement of nerves.

Distant metastasis, though rare, has been reported and described in detail. Metastasis may be to lymph nodes, liver, lungs and to subcutaneous tissues, and apparently occurs both by lymphatic channels and by the blood stream. Stewart's case in 1922 had metastases in the buttock and in the scapular region. Willis found metastases in 2 of his 5 cases, one of them having blood-borne metastases in many organs and the other hepatic metastases.

When Graf described his case with multiple metastases in 1944, there was a total of 10 cases with metastases in the literature. One of the 6 cases described by Crawford in 1958 had pulmonary metastases. There were no cases which have so far developed metastases in the present series, and Dahlin and MacCarty (1952) found none in their 59 cases.

#### *Clinical Features*

The clinical features of chordoma will obviously vary according to the site of the tumour.

The basisphenoid region is the second most common site for these tumours to arise. The clinical features in this situation are variable. They may be those of a slowly growing tumour, gradually infiltrating upwards from the base of the skull and causing nerve palsies and increased intracranial pressure, and there may be no evidence of any spread downwards into the nasopharynx. Until a histological diagnosis is made they may be indistinguishable from other tumours arising in this situation, such as craniopharyngioma or even an intracranial extension of a carcinoma of the nasopharynx hidden in the fossa of Rosenmüller.

I am indebted to Dr. S. P. Meadows and Sir Stanford Cade for the details of a patient who was under their care and who exemplified this type of tumour.

*Case I.*—Male, aged 54, admitted to the Westminster Hospital in April 1949. In September 1947 he developed diplopia and pain in the right eye with occasional twitching of the right side of the face. In March 1948 slight proptosis of the right eye was observed with complete right VI nerve palsy. On admission he was found to have right VI, IX, X and XI cranial nerve palsies. Radiographs showed destruction of the posterior clinoids on both sides and of the dorsum sellae and the tip of the right petrous bone.

He was treated by X-rays on several occasions in 1949 and 1950, with improvement, and by the 10-gram telerradium unit for recurrence in 1954. His condition deteriorated and he died in March 1955, seven and a half years after his symptoms began.

At post-mortem examination of the head and contents after removal of the cerebral hemispheres, a large nodular, well-circumscribed tumour was seen occupying the medial part of the right middle fossa and basisphenoid region. Laterally the tumour was entirely extradural, the dura being stretched over it but not eroded. Posteriorly it was pushing the brain-stem backwards, deeply indenting the anterior aspect of the pons. The sella turcica could barely be defined on the surface of the mass which was growing upwards and pushing the optic chiasma to the left of the mid-line. Both optic tracts were attenuated and soft and tightly stretched over the upper surface of the growth.

On removing the tentorium, cerebellum and dura mater, the growth was seen firmly attached to the base of the skull and was 6 to 7 cm. in diameter. The bulk of the tumour lay on the right of the mid-line, and in colour it varied from green to white, on the whole appearing vascular.

It was difficult to identify the cranial nerves on the right side of the brain-stem, but those that were identified were seen to be thinned by stretching. The anterior surface of the left petrous bone had a slightly worm-eaten appearance, but the only bone to be extensively destroyed was the basisphenoid bone.

Fig. 3, illustrating the macroscopic appearance of a chordoma, is taken from this case.

*Histologically* there was some modification, presumably due to irradiation, in the form of fibrosis and large cells with bizarre, hyperchromatic nuclei, but the growing margin, in-

cluding that in bone at the base of the growth, showed the typical branching strands of physaliphorous cells and the production of mucin.

3 of the 8 patients with basisphenoid growths presented with swelling in the nasopharynx (Cases II, III and IV), and one with a tumour both inside the cranium and in the nasopharynx (Case V).

*Case II.*—Woman, aged 63, who had nasal obstruction for many years and was found to have a fleshy tumour growing from the vault of the nasopharynx. This was removed by diathermy after transpalatal approach by Mr. Douglas Ranger in June 1958, and was found to be a chordoma. At present there is no sign of recurrence.

*Case III.*—Man, aged 33, who had a three months' history of nasal obstruction and deafness in the left ear. After biopsy he was treated by supervoltage irradiation with the Theratron cobalt unit for a mass filling the nasopharynx. There was marked regression of the tumour when his treatment finished three months ago.

In neither of these cases was there any radiological evidence of bone involvement despite attempts to demonstrate it by special views and tomographs.

*Case IV.*—Woman, aged 29, admitted to the Middlesex Hospital in June 1933. She had a smooth, slightly lobulated tumour in the posterior wall of the nasopharynx. A little gelatinous material was obtained on aspiration. X-ray examination of her skull showed no evidence of bone erosion, though the posterior part of the sphenoidal sinus was opaque. On frozen section the tumour was stated to be a nonmalignant mucous gland tumour, though Professor R. W. Scarff at the time considered that it was a chordoma.

She was treated by radium needle implantation with regression of the tumour, but a year later was readmitted and died. Autopsy showed an intracranial chordoma which indented the inferior margin of the pons.

*Case V.*—Man, aged 37, referred to Mount Vernon Hospital from the Westminster Hospital in April 1955. He had a year's history of increasing pain in the right side of the forehead and face, and had been under observation for six months. He had a left VI nerve palsy and gradually developed a V and III nerve palsy. There was a tumour in the right side of the nasopharynx.

X-ray examination showed a partly calcified tumour in the mid-line, obliterating the pituitary fossa (Fig. 5). A left carotid arteriogram showed displacement of the carotid siphon but no blood supply to the tumour.

The mass in the nasopharynx was found to be cystic and was punctured and material removed for histology. The histological report stated that it was not particularly suggestive of a chordoma and that it was probably mucinous degeneration in a connective

capsule and basal ganglia on this side. The cut surface of the tumour was gelatinous with a bluish tint, flecked with haemorrhage. It was thought that the haemorrhage might have been caused by regression of the tumour as the result of irradiation. Histologically several sections were examined and finally the typical structure of chordoma with physaliphorous cells was found.

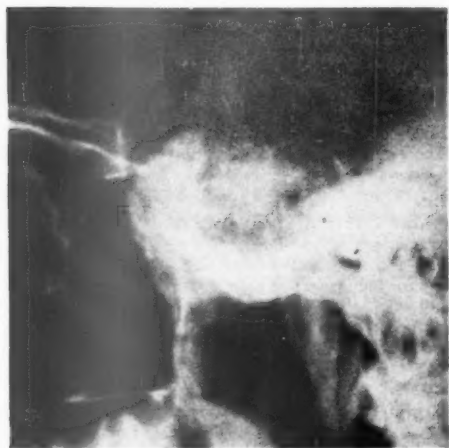


FIG. 5 (Case IV).—Partly calcified chordoma of basisphenoid region.

tissue tumour. He was treated by the Theratron telecobalt unit, receiving 7,200 r over fifty-seven days. Three days after completion of treatment he had an intracranial accident, and died two weeks later.

Considerable interest was taken in the diagnosis of this condition because, although we had made a provisional diagnosis of chordoma, the biopsy from the nasopharynx failed to confirm this and it was considered that the dense calcification seen on radiographic examination made this diagnosis unlikely.

At post-mortem examination of the head and contents there was a massive tumour 6 cm. in its longest diameter occupying the sphenoidal region in the mid-line, invading the pituitary fossa and surrounding the optic nerves. The dura was elevated over the rounded contours of the tumour. It was bulging into the nasopharynx as a smooth, flat, domeshaped swelling. An extension spread into the right middle cranial fossa, infolding itself deeply into the temporal lobe of the brain; a large recent haemorrhage surrounded this extension within the temporal lobe, pressing on the internal

#### *X-ray Appearances*

The X-ray appearances of chordoma are usually of a lesion which causes irregular destruction of the affected bone, bursts through the cortex and forms a soft-tissue mass extending out from the bone. The edges of the bone where the tumour has burst through may be expanded outwards and flakes of bone may be carried out in the soft tissue tumour. Arteriography shows displacement of vessels by the tumour but no new blood supply to the tumour mass. Calcification in the tumour has been described and in fact is stated as one of the four cardinal signs of sacrococcygeal chordoma by Hsieh and Hsieh (1936). Dahlin and MacCarty (1952) found it in 2 of the 15 clivus tumours in their series and Wood and Himadi (1950) observed it in 6 of 7 clivus tumours. Mabrey (1935), however, stated "the lesion is not a bone tumour and bony proliferation is not to be expected".

Only one patient in the present series showed extensive calcification. The others had little or none, and I think a more typical example of spheno-occipital chordoma with intracranial spread is the patient illustrated in Fig. 6, at present under the care of Mr. Valentine Logue.

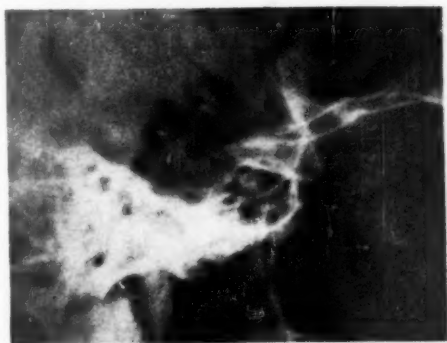


FIG. 6.—Chordoma of basisphenoid region. Bone destruction. Soft-tissue tumour outlined by encephalography.

There is bone destruction and no new bone formation.

The clinical features of vertebral chordoma depend on the site of origin of the tumour, not only on the level of the vertebra involved but also on the direction of spread. Pain is usually the earliest symptom, and it may be local at the site of origin of the tumour or be referred along a nerve distribution and be accompanied by tingling and paræsthesia. There may be the typical signs of pressure on the spinal cord as seen in other types of tumour, with nerve palsies and ultimately paraplegia. On X-ray examination there may be collapse and distortion of the vertebrae. A soft-tissue mass may protrude, most frequently anteriorly but sometimes at the side of the vertebrae or even posteriorly, and will cause symptoms which will vary according to the level of the spine which is involved.

These features, as far as the cervical region is concerned, are exemplified in the following 3 cases:

*Case VI* (Fig. 7).—Woman, aged 31, admitted to the Westminster Hospital in 1950. For two and a half years she had persistent pain in the neck. In September 1949 she developed a lump in the right side of the neck. After biopsy she was treated by 200 kilovolt X-ray therapy and the 10-gram telerradium unit, receiving over three months a tumour dose of approximately 5,000 r. There was slow but

gradual improvement in pain, and the tumour decreased to about one-third of its former size. She died, however, in May 1952.

*Case VII*.—Girl, aged 8, admitted to Mount Vernon Hospital in October 1956. She was in normal health until one month before, when she developed pain in the right hypochondrium. She had marked wasting of scapular muscles and both sternomastoids, and of her arms and forearms. There was weakness of all groups of muscles in both legs. X-ray examination showed erosion of the spinous process and right lateral mass of the fifth cervical vertebra. Biopsy showed chordoma. She was treated by the four million volt linear accelerator to a tumour dose of 5,000 r over thirty-five days, and after an initial favourable response relapsed and died seven months later.

*Case VIII* (Fig. 8).—A man aged 41 in April 1954 complained of swelling in his neck, that his collars were too tight and that he had slight discomfort on swallowing and slight pain in the right arm with pins and needles in the fingers. He was found to have a hard mass behind his larynx, pushing his larynx forwards.

After biopsy he was given a course of treatment with 200 kV X-rays to a tumour dose of 4,750 r, following which there was a decrease in the mass and he felt much better. In March 1955 he was referred to Mount Vernon because of a return of pain and tingling in his hand, and he was treated by the



FIG. 7 (*Case VI*).—Chordoma involving 2nd cervical vertebra with soft-tissue tumour extending into pharynx.



FIG. 8 (*Case VIII*).—Chordoma of fifth cervical vertebra with soft tissue mass pushing forward the posterior pharyngeal wall and displacing the larynx.

Theratron cobalt unit. It was not possible to see his larynx on indirect laryngoscopy because of distortion by the tumour mass. There was regression of the tumour and his cords could be seen with the laryngeal mirror. After initial improvement in his pain and tingling he began to deteriorate, developed paraplegia and died.

*Case IX* was the only patient with a chordoma in the thoracic region. He was admitted to the West Middlesex Hospital under the care of Mr. Iltyd James in September 1947, with symptoms and signs of a spinal cord tumour. The physical signs suggested a lesion of the third thoracic segment. After laminectomy he was found to have extensive thickening of the dura mater from the first to the fifth thoracic vertebrae. The extradural mass was found to be spreading a considerable distance up and down the extrathecal space. Sufficient of the tumour was removed from the posterolateral and anterior aspects of the cord to relieve pressure. This was found to be a chordoma with mucoid degeneration. Following the operation there was some return of power in his legs. He was given post-operative treatment with X-rays at 200 kV with an estimated dose at the lesion of 3,650 r. He had been in a home for paraplegics and at present, nearly twelve years later, he is reported as unchanged and able to do a full day's work in a factory.

*Case X*, the patient with a lumbosacral tumour, was a woman aged 29 when admitted to the Middlesex Hospital in 1953 with a most extensive lesion. At the age of 12 she fell down some steps and shortly afterwards developed severe pain. X-ray examination showed no abnormality, but the pain persisted. She had her spine manipulated as she became unable to straighten her legs. At the age of 17, foot-drop developed and she lost sensation in her feet. She later lost control of her bladder and her bowel. At the age of 24 she was manipulated by an osteopath who, after five years, recommended her to seek advice at the Middlesex Hospital.

In June 1953, after extensive investigations, no treatment was advised as we considered that conventional X-ray therapy offered no hope of improvement. She was able to control her bladder and bowel function and was able to get about with crutches. X-ray examination (Fig. 9) showed osteolytic areas in the third, fourth and fifth lumbar vertebrae extending anteriorly from the posterior aspects of the bodies. There was a similar appearance of the upper two-thirds of the sacrum. There is well-marked kyphosis at the fourth lumbar vertebra, which shows considerable destruction.

In 1954, when we had treated several cases of chordoma with the Theratron cobalt unit, I decided to treat this patient, with the object of at least preventing further extension of the tumour. A biopsy was carried out from the lumbar area, as it was presumed to be the area of most recent extension.



FIG. 9 (*Case X*).—Extensive lumbosacral chordoma.

Although typical physaliphorous cells were not seen the appearance was highly suggestive of chordoma.

She was treated by the Theratron at Mount Vernon, receiving a tumour dose to the lumbar spine of 5,600 r over forty-five days with a cycling rotation technique, and two months later further treatment was given to the sacral area to a tumour dose of 5,800 r over fifty-five days with a similar technique. It is now four years since the treatment was given and there is no appreciable change in her symptoms. She is still at work as a telephonist, over 21 years since her first symptoms began.

The cases of sacrococcygeal chordoma have formed the largest group in this series, as has been the case in all the larger reported collections. A clear clinical picture of the condition can be built up from a study of the 13 cases in this group. In all of them without exception, pain was the first symptom of which they complained. It was described as a gradually increasing aching pain, and its distribution varied from the lower back, the buttocks, the hips, over the sacrum to extension down one or both legs. It was usually followed by the recognition of a lump, either externally or within the pelvis, by reason of its size causing pressure and interference with micturition or bowel action. Later there develops loss of control over bladder and bowels due to interference with their innervation and, later still, there

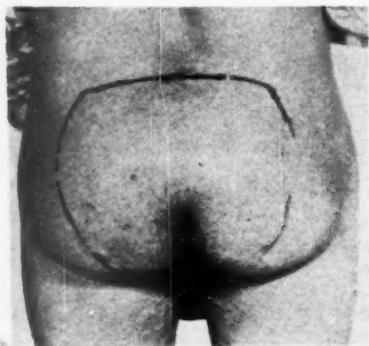


FIG. 10.—Sacrococcygeal chordoma. Tumour involving sacral region and both buttocks.

may develop nerve palsies with perhaps foot drop and weakness of legs.

The tumour itself, having eroded bone, in most cases extensively, appears to push the soft tissues aside and to compress them rather than to infiltrate into them. When an external mass is present it may appear in the mid-line over the sacrum, particularly in its lower part, or it may appear in either buttock, or there may be a generalized swelling of the whole region of sacrum

and medial parts of both buttocks. It is generally firm, smooth and elastic to feel, rather than stony hard. It is not painful and there is no tenderness and no signs of increased vascularity (Fig. 10).

The tumour within the pelvis can be felt, sometimes of vast extent, almost filling the pelvis and pushing the rectum forward. It fills up the concavity of the sacrum and may arise from the mid-line or from either side. In all the cases which I have observed it is smoothly irregular and lobulated and has a definitely firm, elastic feel. It is firmly fixed posteriorly and invariably too large and too high for the examining finger to reach more than the lower part of it. The rectal wall, although pushed forwards, is freely mobile and not attached to the tumour. Radiologically there is gross destruction of the lower part of the sacrum and coccyx with irregular edges of the destroyed bone and areas of rarefaction extending upwards into the sacrum where the tumour is infiltrating. There may be a large soft-tissue shadow which causes difficulty in recognizing details of the edges of the destroyed bone. In the lateral view the sacrum is expanded with irregular areas of rarefaction. Arteriography shows displacement of vessels and no new vessel formation (Figs. 11 and 12).

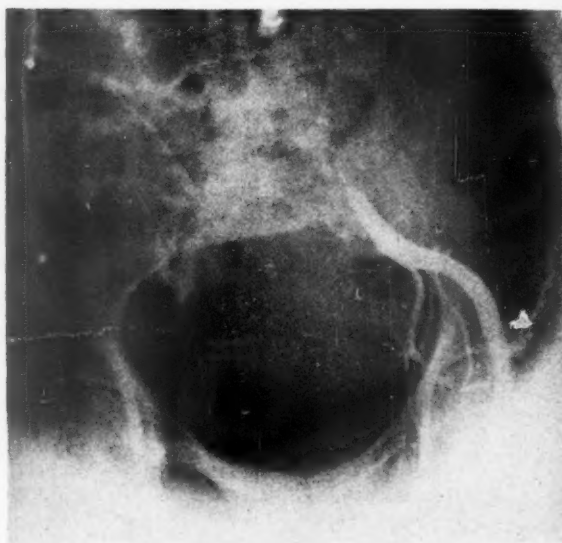


FIG. 11.—Sacrococcygeal chordoma. Extensive destruction of sacrum. Massive soft tissue tumour. Displacement of blood vessels and no new blood vessel formation.



FIG. 12.—Sacrococcygeal chordoma. Partial destruction of sacrum.

Hsieh and Hsieh (1936) described four cardinal features: (1) Expansion of the sacrum in the lateral or anteroposterior diameter; (2) areas of rarefaction or destruction that tend to be loculated; (3) trabeculation of the undestroyed bone; (4) areas of calcification in the tumour.

Some illustrative examples are the following:

*Case XI.*—A man aged 53 who came to the Middlesex Hospital in 1939 with a recurrent chordoma. Following a six years' history of pain he had partial removal of a sacral tumour in 1935, followed by a radium needle implant and later X-ray therapy. He had a mass the size of a football in the right buttock extending across the midline to the left buttock. It was hard, but cystic areas were palpable. At the Middlesex Hospital he had X-ray therapy with palliative intent, gradually deteriorated and died twelve years after the development of his first symptoms.

*Case XII.*—Man, aged 64, referred to the Middlesex Hospital in 1943. He had a six months' history of lumbago. While his doctor was removing a chronic olecranon bursa under local anaesthesia the patient complained of the discomfort of the operating table. He was turned over and a softish tumour the size of an apple was found over the sacrum. This was thought to be a lipoma and removal was attempted forthwith. It was found to be a cystic tumour which shelled out easily, but large quantities of friable material came away at the same time with small pieces of bone. The patient developed urinary retention. In 1943 he was given 200 kV X-ray therapy, 5,250 r in forty-one days, and remained well until 1948. He was then given a further 5,000 r in sixty-six days for a recurrence of the tumour. He gradually deteriorated and died with loss of bladder function, uræmia and infection in 1952, nine years after his first symptoms began.

*Case XIII.*—Man, aged 58, referred to Mount Vernon by Sir Stanford Cade in February 1955. A year previously he had pain in the region of the sacrum, and in December 1954 he first noticed a swelling over the sacrum to the right of the mid-line and an area of numbness between the swelling and the anus. On rectal examination he had a lobulated semicystic tumour the size of a tangerine, pushing the rectum forwards, and there was a soft diffuse mass overlying the right half of the sacrum. X-ray showed typical destruction of the lower half of the sacrum towards the right side. Biopsy showed chordoma. He had treatment by the Theratron cobalt unit, 6,500 r being given over fifty days, with complete rotation technique. He is well at the present time with no symptoms and no tumour palpable, four years since his treatment.

*Case XIV.*—A woman aged 55 came to the Middlesex Hospital in 1951 complaining of low back pain on bending and stretching. X-ray examination at that time showed no bony lesions. The pain became worse and extended into the right buttock by 1955. In 1956 she became obstinately constipated

and developed pruritus. An X-ray taken in August 1956 showed some destruction of the sacrum. By January 1957 she had gone through the stages of stress incontinence to complete incontinence of urine.

In April 1957, when I first saw her, she had pain down her right leg and swelling of both buttocks. After biopsy, which showed chordoma, she was treated at Mount Vernon by the Theratron to a dose of 6,300 r in thirty-nine days with cycling rotation. She had already had a colostomy and then had deviation of her urine into an ileal loop carried out by Sir Eric Riches.

Although the tumour regressed she still had foot-drop and severe pain, which was treated by chordotomy by Mr. Valentine Logue. At present she is bedridden and her nerve involvement and consequent muscle weakness are too severe for any progress to be made in rehabilitating her. I suspect that she may be developing a recurrence.

There have been two interesting cases in this group who had second primary tumours of a different nature (Cases XV and XVI).

*Case XV.*—Man, aged 49, treated by nephrectomy by Sir Eric Riches in 1952 for a carcinoma of the right kidney with post-operative X-ray therapy. He had complained of low back pain for some years and had had a manipulation for this. In 1956 his pain was worse and a swelling was felt over the right side of the sacrum. It was thought to be a metastasis from the kidney and a biopsy was taken. This proved to be a chordoma. He was treated by the Theratron but was unable to complete the course owing to infection of the biopsy wound, and he died six months later.

*Case XVI.*—Woman, aged 42, referred to Mount Vernon Hospital by Sir Stanford Cade in March 1957. She had an extensive sacrococcygeal chordoma with low back ache and incontinence of urine and faeces. She had already had a colostomy and a biopsy which showed chordoma. She was treated by the Theratron to a dose of 7,500 r over sixty-two days by full rotation. At that time she was advised to have deviation of her urine into an ileal loop, but she refused. The tumour regressed and she gradually regained control of her bladder so that it functioned normally. In September 1958 she had a return of pain in her ischial tuberosities and was found to have a stricture of her rectum. This was proved to be an adenocarcinoma of the rectum and was removed by Sir Ralph Marnham. Her convalescence was uneventful, except that she was slow in healing, but she is well at present and retains her bladder function.

#### Summary of Clinical Features

Tumours in the speno-occipital region may present with intracranial tumour, with nasopharyngeal tumour or both, and there is no particular symptomatology of chordoma to distinguish it from other slowly growing tumours in these regions.

Patients with these tumours are of a somewhat younger age group than those with sacrococcygeal chordomas and they do not live as long, owing to nerve involvement.

In the vertebral region, the least common site, there is pain, involvement of the cord by pressure or vertebral collapse and consequent nerve palsies, and there may be a soft-tissue tumour, protruding in any direction, but most frequently anteriorly. In the sacrococcygeal region there is pain and a tumour either protruding posteriorly or into the pelvis, or both, and sometimes of great volume. It is lobulated and semifluctuant. There is extensive bone destruction of the lower end of the sacrum and coccyx. There may be nerve involvement causing paralysis of bladder and rectum and of the nerves supplying the lower limb. It is the most frequent site of chordoma; the patients are mainly over 40 and they tend to live for many years, even with active growth present.

#### Treatment

In all publications on the subject it is recognized that to devise any curative treatment for chordoma is a matter of great difficulty. Complete surgical ablation is hardly ever possible owing to the situation in which these tumours arise. It is not possible to remove the base of the skull and it is not possible to remove the sacrum in its entirety. Partial excision is an excellent palliative, although there is usually recurrence within a few years, but many patients have been kept going for a number of years by repeated partial excisions. The case reported by Stewart in 1922 and operated on by Moynihan lasted nineteen years from the beginning of symptoms.

At the Mayo Clinic there is now a programme of attempting a more radical surgical removal of the sacrococcygeal tumours, with wider ablation of the sacrum (MacCarty *et al.*, 1952). The sacral nerves are dissected out from the tumour mass and preserved. Owing to the rarity of the condition and its slow rate of growth, it will take some years before this procedure can be evaluated.

In this series there are a number of cases who have been treated by surgery. One patient had partial removal of a tumour in the clivus region in 1952, and excellent palliation was obtained for four years, when the tumour began to grow again, and he has been referred for radiotherapy. There is in addition Ranger's patient with nasopharyngeal presentation and no evidence of intracranial spread or bone involvement, but this is only nine months ago.

Case XVII, a girl aged 16, was the one patient with a lumbar spine chordoma. She was quite well until

aged 11 when she had a fall on her lower back followed by pain in the legs and sphincter disturbances. Two to three years later she began to develop deformity of the spine, which continued to increase in spite of treatment. Her legs became weaker and she was unable to walk unaided. In 1949, Miss Diana Beck performed a laminectomy and removed a tumour of the cauda equina; the histological examination showed it to be a chordoma. Six years later she was apparently unchanged; she was able to get about with crutches and had marked sensory loss in both legs.

It is, however, the possibilities of radiotherapy which have been my chief interest in treatment in the cases which I have seen. The majority of publications on the treatment of chordoma, when the subject is mentioned at all, begin with the statement that these tumours are radio-resistant and that radiotherapy is of no value, and I believe that the majority of radiotherapists are of the same opinion.

The reports from Boston (Mabrey, 1935) state, however, that radiotherapy has been of value as a palliative in the relief of pain, and Dahlin and MacCarty (1952), from the Mayo Clinic, cite 2 cases who had complete remission of symptoms for five and a half years, and for six and a half years, having been considered inoperable and having been treated by radiotherapy alone. I became impressed with the regression that was obtained in one or two cases when conventional 200 kV X-rays were given to high dosage, and determined when supervoltage became available to attempt to treat other cases if I could find them. The first and most spectacular of these results is one which I have included in this series of 29 chordomas, although there is no histological evidence of the diagnosis. It is the only case in the series which has not a histological diagnosis.

Case XVIII.—In April 1941 a man aged 31, recently qualified in medicine, sought advice at the Middlesex Hospital. He had had calcified tuberculous glands in his neck for many years. For seven years he had been conscious of a mass projecting forwards into the pharynx from the left posterior wall. He had developed a sudden pain in his neck which limited movement of his head. There was a retropharyngeal mass pushing his palate forward, which was thought to be fluctuant, and a provisional diagnosis of tuberculous abscess was made. The mass was aspirated and some mucinous material obtained. It was thought to be incompatible with the contents of a cold abscess, and there was a hard tumour remaining. A clinical diagnosis of chordoma was made.

X-ray examination showed a retropharyngeal mass with some irregular bony destruction of the body of the second cervical vertebra (Fig. 13A). He was treated with 200 kV X-rays to a tumour dose of 9,200 r, including 5,200 r by direct intrabuccal



FIG. 13A (Case XVIII).—1941: Irregular decalcification of second cervical vertebra with soft tissue mass pushing forward the posterior pharyngeal wall.

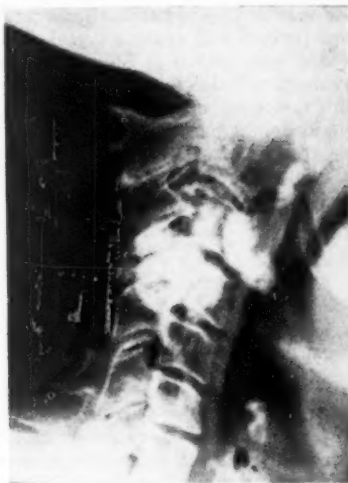


FIG. 13B (Case XVIII).—1955: Disappearance of soft tissue tumour. No recalcification of second cervical vertebra.

application over forty days. Three months later, in October 1941, a further tumour dose of 2,800 r was given over eighteen days and in April 1942, a further tumour dose of 1,500 r in ten days.

The patient is now well and continues his work in a specialized branch of medicine. X-ray examination (Fig. 13B) shows that the destroyed vertebra has not calcified, and he continues to wear a plastic support.

After his heavy radiation dose he has marked skin changes on his neck.

If the diagnosis were mistaken and this condition had been a tuberculous abscess, the other most possible diagnosis, I would have expected that the heavy dose of radiation would undoubtedly have aggravated the condition. It is now eighteen years since he was treated and twenty-five years since his symptoms began.

*Case XIX*, a woman aged 36, was admitted to the Middlesex Hospital in November 1954. For six months she had had pain down the posterior surface of the right thigh, gradually getting worse and spreading down the leg to the foot. She was found to have a smooth, firm, rounded tumour projecting into the rectum from the right. It did not extend to the mid-line and was firmly attached to the sacrum. The upper surface could just be reached by the finger. There was also a firm tumour in the right buttock. After biopsy an attempt was made to carry out a hind-quarter amputation but it was found that the tumour extended widely across the front of the sacrum upwards, almost to the brim of the pelvis, so that the sacro-iliac notch was completely obliterated on its inner aspect and the operation was abandoned.

She was treated by the Theratron cobalt unit at Mount Vernon receiving a dose of 6,100 r in fifty-two days with complete rotation technique. By the end of the treatment the tumour in the buttock had disappeared and the rectal tumour was no longer palpable.

At the beginning of treatment she had pain in the right foot and ankle which prevented her putting her foot to the ground. X-ray examination showed a patchy osteoporosis consistent with Sudeck's atrophy. Vigorous physiotherapy was continued after the completion of her radiotherapy. The pain in her right foot disappeared and she began to walk normally. We have wondered at the cause of the Sudeck's atrophy and consider that it might have been caused by damage to sympathetic nerve supply during the course of the attempted hind-quarter amputation.

She is now well, with no sign of recurrence, over four years since her radiotherapy, but is again walking badly because of severe arthritis of her right hip also due, I believe, to the damage to her nerve supply.

Histologically this is not completely definite, but I believe she had a chordoma and have counted her in this series.

When dealing with a tumour which is slowly growing and which rarely metastasizes, in which the natural history of the disease extends over many years, it takes many cases and a long period of time to arrive at definite conclusions as to the curative value of any method of treatment. Some of the cases which I have described and others who had tumours in the sacrococcygeal region, who are now alive and well without sign of

disease, may develop recurrence in the future, but of the 8 patients with sacrococcygeal chordomas who have been treated at Mount Vernon with supervoltage radiation since 1954, 6 are at present without symptoms or signs of the disease, 1 of these 6 having had a second course of treatment for recurrence a year ago, after freedom for four years. Of the remaining 2, 1 has probable recurrence after two years' freedom, and 1 is too early to evaluate.

I hope I have shown that radiotherapy has some value in the treatment of chordoma. I consider that, at least as a palliative, it should be given in preference to partial operation in sacrococcygeal tumours.

Supervoltage radiotherapy, and in this series it has been mainly by the Theratron cobalt unit, has given the opportunity of delivering the high dose necessary without excessive damage to the overlying and surrounding tissues. Rotational techniques are also particularly appropriate, as we believe that in this way we can more accurately limit the dose to the volume of tissue required. This is of considerable importance as there must be some danger of causing transverse myelitis, which has been described as the result of irradiation, if excessive dosage is given to the spinal cord.

With supervoltage irradiation, given over a prolonged period of time, and by limitation of the volume of tissue irradiated, it may be possible to operate with safety in some cases, even after such a heavy dose as 7,500 r delivered over sixty-two days, as had to be done in the case of the woman who developed carcinoma of the rectum (Case XVI).

I would like to acknowledge with gratitude the help that I have had from many clinical col-

leagues, especially Sir Stanford Cade, and from Professor R. W. Scarff, Dr. A. C. Thackray, Dr. A. D. Thomson, and Dr. R. E. Cotton of the Bland-Sutton Institute of Pathology, from Dr. G. W. S. Andrews of Mount Vernon Hospital Pathology Department, from Dr. Campbell Golding and Dr. H. S. Murray, and from Mr. M. S. Turney of the Photographic Department of the Middlesex Hospital, who has produced my slides.

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## Section of Physical Medicine

President—KENNETH LLOYD, M.R.C.P.

### Meeting

December 10, 1958

THE thirteenth Samuel Hyde Memorial Lecture was delivered by Professor J. Z. YOUNG (London); his subject was **Nerve Regeneration**.

### Meeting

May 13, 1959

### Arthrogryposis Multiplex Congenita

By D. Y. MACKENZIE, M.D., M.R.C.P., D.C.H.

London

ONE of the most disabling of the congenital abnormalities with which we have to deal is the condition of arthrogryposis multiplex congenita. It is characterized by multiple rigid joint deformities which are present at birth (Fig. 1). The condition was first described by Otto in 1841. In 1905 Rosencranz described a group of cases of club hand and contractures of the upper extremities and introduced the name arthrogryposis, meaning a curved or crooked joint. Many have objected to the name arthrogryposis multiplex congenita because in some of the cases the affected joint is persistently straight and cannot be bent; because it suggests that the condition is one primarily of joints and does not indicate the important changes in the muscles; and because it contains a mixture of Latin and Greek. Nevertheless it has a certain phonetic charm and has persisted in the literature. Most of the reports have been based on only a few cases with resultant difficulty in drawing any concise picture of the aetiology and natural history of the condition. Two more comprehensive reports have appeared in the American literature, by Kite (1955), who reviewed 54 cases he had seen personally, and by Mead *et al.* (1958), who reported on 40 cases seen at the Hospital for Crippled Children in Chicago. There has been no comparable review in this country. The present study is based upon 37 cases seen at the Hospital for Sick Children, Great Ormond Street, during the past twenty-two years. The purpose was to see if any conclusions could be drawn which would aid in the understanding and management of the disorder.

It has long been considered possible, and by many likely, that arthrogryposis is caused by a chromosomal defect. Kite found 3 arthrogrypotics with arthrogrypotic children, in 2 cases the mother being affected and in 1 the father; in

6 cases (11%) there were deformities in ancestors. In the present series there was no history of deformities in the families of the affected children and in no case was there any associated disorder suggesting a hereditary aetiology; this is in agreement with the cases reported by Mead *et al.*, where careful investigation failed to reveal any



FIG. 1.—Arthrogryposis multiplex congenita.

similar congenital anomaly in the families of the 40 children studied. One of the children seen at Great Ormond Street was a twin, the other twin being perfectly normal. Hillman and Johnson (1952) reported two sets of identical twins in which one child of each set was normal and the other arthrogrypotic. Two similar twin pregnancies were reported by Mead *et al.* and three

sets of twins each with one affected infant by Kite. This would appear to refute the theory that the disease is hereditary. It also casts doubt on the importance of certain other intra-uterine factors such as infections and toxic and circulatory influences which are unlikely to affect one twin and not the other.

An interesting feature arises in this series in relation to the mother's condition during pregnancy. In 8 cases the mothers stated that they were smaller than during preceding pregnancies, and in two other cases, both primiparae, the mothers stated that they were small during the pregnancy. Movements were less noticeable and in 4 cases the pregnancy was more uncomfortable. 4 considered that they were rather large, but 2 of these had no preceding or subsequent pregnancy with which to compare their size. In the remainder no specific comment was made in relation to size, but 2 complained of feeling unwell in comparison with other pregnancies. In 2 cases there had been a previous miscarriage and in 2 cases a threatened abortion had occurred. One mother stated that there had been slight blood loss during the first four months of the pregnancy and another had a threatened miscarriage at the thirty-second week. There was no history of significant infections or exposure to X-rays during the pregnancy. One mother had toxæmia and renal trouble but the pregnancy went to full-term. Abnormal pressure was felt in the side in one case, and in the chest in another. Two mothers complained of discomfort after a breech was turned towards the end of pregnancy.

The gestation period was normal in all cases except for one in which labour occurred two months before the expected date of delivery, and in only 2 other cases were the infants premature as assessed by birth weight. One infant weighed 5 lb. at birth and the other, the arthrogryptic twin, 4½ lb.

The mothers' ages, where stated, were within the normal range and there was no evidence that the condition occurs more frequently at the extremes of the reproductive cycle.

In 11 cases the infant resulted from the first pregnancy. 8 occurred in the second, 7 in the third, 4 in the fourth, 1 in the fifth and 1 in the sixth pregnancy. In 5 cases the order of birth was not stated, but it seems probable that there were no preceding siblings.

Breech presentation occurred in 7 cases and face presentation in one. In one case a Cæsarean section was performed because of impaction of the head and the mother was found to have a bicornuate uterus. Labour and delivery

were otherwise uncomplicated in all cases except one where forceps had to be used following deep transverse arrest.

Two infants required oxygen at birth because of difficulty in establishing respiration. The condition of the remaining infants was normal except that the limb deformities were obvious at birth apart from the most mildly affected cases.

There may be involvement of all four extremities or of one or two. The changes tend to be symmetrical. There is marked wasting due to diminished muscle substance and considerable limitation of joint mobility due to increased fibrous tissue about the joints. The joint changes are characteristic in that, despite the rigidity, a few degrees of movement are present, and this is quite free and painless. The muscle changes may be such that activation of the joint is almost impossible and the movement entirely passive. The skin and subcutaneous tissues may be involved but bone is unaffected except for secondary influences.

The legs and arms were involved in 28 cases in the present series, the legs alone in 4 cases, and the arms alone in 5 cases. No case was unilateral.

The most common deformity was talipes equinovarus which was present in 29 cases. In 1 case talipes equinovarus of the right foot was associated with calcaneolavagus of the left foot, and in 1 case with equinovaglus of the left foot. The knees were involved in 26 cases and the hips in 17. A flexion deformity is usual at the knee but in 7 cases the knee was in complete extension. The shoulders were involved in 17 cases with movement being limited to less than a right angle. 25 cases had involvement of the elbow, rigidity in flexion being commoner than rigidity in extension. The wrists and fingers were involved in 29 cases, the deformity being generally one of flexion. The fingers are characteristic in appearance being tapered with smooth skin and are likened to a bent wax candle.

*Associated deformities.*—Congenital dislocation of the hip, which is generally reported as a common association, was present in 6 cases, being bilateral in 5 and unilateral in 1. 2 infants showed X-ray changes at the hip-joints, 1 having shallow acetabulæ and the other dysplasia and subluxation. Associated deformities included cranio-stenosis in 1 case, congenital heart disease (P.D.A. and V.S.D.) in 1 case, syndactyly in 1 case and tongue-tie in 1 case. One infant had an associated osteogenesis imperfecta with multiple fractures. Multiple deformities were present in 2 cases. One of these infants had micrognathos, a cleft palate, a deformed right auditory meatus



FIG. 2.—Arthrogryposis with associated deformities.

and an absent left sternomastoid muscle (Fig. 2). The other had micrognathos, Sprengle's shoulders, scaphocephaly and a sternomastoid tumour. Congenital laryngeal stridor occurred in this and in one other case. One infant had a deformed chest and 2 had herniæ, 1 inguinal and 1 umbilical, requiring surgical treatment.

An impression has been given by many of the reports in the literature that mental deficiency is frequently associated with arthrogryposis; this is incorrect. In the present series only 2 cases showed mental retardation, a figure in agreement with the Chicago report where only 2 of the 40 patients were considered below normal in intelligence.

No post-mortem material has been available for study in the present series. A biopsy was performed in 2 cases, both specimens showing small atrophic muscle fibres with reduction of sarcoplasm and a spurious increase of nuclei. Adipose and fibrous connective tissue was increased (Fig. 3).

Laboratory investigations, where undertaken, revealed no significant abnormality.

There were 2 deaths during infancy. 1 infant with involvement of all limbs, bilateral dislocation of the hips and congenital laryngeal stridor had recurrent chest infections and died from pneumonia at the age of 6 months. Another infant, with moderate involvement of all the limb joints, developed the typical picture of infantile progressive muscular atrophy and died at the age of 6 months. Difficulty was experienced with the feeding of 1 of the cases with multiple defects and the weight gain was slow. The remainder of

these children thrived normally during infancy. Developmental milestones were passed at approximately normal times excepting those activities which were dependent on the arthrogrypotic limbs. Resistance to infection during childhood appeared to be normal although 2 children with involvement of the shoulders showed an increased susceptibility to respiratory infections. Follow-up of the cases observed through childhood revealed no evidence that this is a progressive disorder. Unfortunately there appears to be little spontaneous improvement.

The management of these children is of considerable importance. The normal intelligence must be recognized and every effort made to ensure suitable education and to prevent psychological upsets complicating the physical disabilities. Attendance at an ordinary school may be possible where the disability is slight. In most cases the nature of the disability makes ordinary schooling difficult. In addition to the difficulty experienced in writing and other school work, children with arm involvement may be unable to dress themselves or attend to their own toilet. Attendance at a school for physically handicapped children is usually necessary.

The aim of treatment for those cases with involvement of the lower limbs is to obtain stability, and as good weight-bearing alignment and locomotion as possible. Simple conservative measures have occasionally sufficed in the mildly affected case, but the fibrous thickening around the joints of the average case has usually pre-



FIG. 3.—Biopsy showing typical muscle changes.

vented successful manipulation and the lack of muscles has often rendered a joint useless even though a considerable range of movement was present. The more severe degrees of club-foot have proved intractable, tending to relapse in spite of all forms of management. In general the more rigid the deformity at the start of treatment, the greater the tendency to relapse regardless of the treatment selected. This deformity, however, tends to progress with growth and incorrect weight-bearing and contractures are a common occurrence. Corrective treatment has been started as early as possible in the usual sequence, postponing radical surgical procedures as long as possible to avoid the destructive effect on bone growth.

The knee requires treatment if it is badly deformed or unstable. A weight-bearing position must be achieved as may be possible, with the provision of braces if the muscle power is not sufficient for stability.

Dislocation of the hips is best left alone. Attempts to reduce the dislocation may result in fracture of the neck of the femur. The stiffness which is such an obstruction to successful treatment is beneficial in producing stability. Where instability remains troublesome the gait can be improved by subtrochanteric osteotomies. Mead *et al.* (1958), in their review of surgical management, recorded no case in which a normally mobile stable hip had been obtained in a dislocated arthrogryptic joint.

Surgical procedures have been undertaken in the present series where definite indications for surgery were present. Operations performed have included tendon transplant, wedge resection, tarsal block resection, and triple arthrodesis.

Treatment of the arms must aim at obtaining a position of optimum function and it is important that at least one hand can reach the face.

The results of treatment in general are less satisfactory than in patients with similar deformities resulting from different causes. Unfortunately even after correction of the deformity function may be poor because of lack of muscle power or stiffness. Despite the poor mechanics in many of these children pain has not been troublesome and despite the severe handicap they make a satisfactory adjustment to life.

The outstanding feature in this series in regard to aetiology is the high incidence of pressure abnormalities during the pregnancy. In 10 cases the pregnancy was described as small and in 8 of these the mothers had other pregnancies with which to compare their size. Pressure dimples over bony points (Fig. 4) were observed in 9 cases

and in 2 cases there were depressions in the chest wall into which the deformed arms fitted. In the 2 cases in which a breech was turned by external version, considerable difficulty was experienced in carrying out the manoeuvre in one case and both mothers complained of persistent discomfort following the version.

*Aetiology.*—A variety of theories have been put forward. The degree of severity of the pathological process is variable and accounts, no doubt, for the different views in regard to the essential nature of the condition as expressed by those reporting on only a few cases. Many theories such as intra-uterine periarthritis and virus infections have little to commend them. Hereditary factors as previously mentioned appear unlikely to be of major importance. Sheldon (1932) originally suggested that amyoplasia was the basic abnormality, the joint fibrosis occurring because of the lack of intra-uterine activity. Banker *et al.* (1957) reported a case of arthrogryposis with primary disease of muscle and no abnormality in the central or peripheral nervous systems. Similar cases with pathological studies have been reported by Stoeber (1938), Ullrich (1930) and Howard (1908). It is of interest that in these 4 cases the children all showed a similar clinical picture, of kyphoscoliosis, chest deformity, an abnormality of head posture and a characteristic leg deformity with adduction and flexion of the hips and flexion of the knees. In the present series there were no cases with this clinical picture. Others have felt that the primary abnormality lies in the embryonic nervous system, lack or an abnormality of development resulting in paralysis of the embryonic muscle. Kanof *et al.* (1956) reported their findings on



FIG. 4.—Pressure dimples over bony points.



FIG. 5.—“Wooden soldier” position of arms.

repeated muscle biopsies in 3 patients and a complete post-mortem study in 1 and suggested that the condition may be an infantile form of neuromuscular atrophy rather than a primary disease of either joints or muscles. Adams *et al.* (1953) reported a case of arthrogryposis with involvement of all limbs in which the anterior horn cells had disappeared in the lumbosacral region and were reduced in the upper lumbar, thoracic and cervical regions. A second case with involvement of the lower limbs showed a reduction in number and size of the anterior horn cells in the lumbosacral area. A similar pathological picture has been reported by Brandt (1947).

The muscle loss is not that of joint immobilization and tends to occur in a group of muscles having a common function. This suggests that the joint change is probably secondary to an abnormality in the muscle. In the growing limb bud movements produced by muscle contraction aid in the natural formation of the structure of the joints.

The theory that abnormal intra-uterine pressure was concerned in the production of arthrogryposis has long been considered important by Browne (1957). There appears to be support for his view in the present series. Increase in the hydraulic pressure on the fetus if long continued interferes with the circulation in the limbs. The hydraulic compression affects all four limbs, the greatest effect being in those tissues furthest removed from the heart and in those parts which are unsheltered, normally the legs and feet. The

arms appear to obtain a degree of protection from the large fetal head, although they occasionally become involved and may even be caught in the “wooden soldier” position with extension of the elbows (Fig. 5). The interference in the blood supply to the limbs results in failure of normal muscle development and to secondary thickening and stiffening of the fibrous tissue around the joint.

Certain features emerge from the review of treatment in these cases. The main disability is undoubtedly lack of function rather than structural deformity. A sound physiotherapeutic regime is of the utmost importance in preserving and obtaining the best possible function from the deficient musculature. Manipulation followed by immobilization may improve the position of the joint but unfortunately weakens the muscles and the deformity steadily recurs. Surgery must be undertaken only after careful consideration of the nature of the disability and the aim must always be to enable the patient to use the limbs to the best possible advantage. Deformity and limitation of movement are of much less importance than the total functional efficiency of the limb.

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## Rheumatoid Cysts of the Calf

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A CYSTIC swelling in the centre of the popliteal fossa arising from the bursa between the tendon of popliteus and the lateral condyle of the femur, which is usually an extension from the synovial membrane of the joint, is a common occurrence in rheumatoid arthritis (Meyerding and Van Demark, 1943). Cysts arising in the calf or sometimes in other situations round the knee-joint are less common and may present diagnostic difficulties. There is surprisingly little mention of this complication of rheumatoid arthritis in the literature.

### CASES

*Case I.*—Woman aged 34, seen June 1957. She had suffered from rheumatoid polyarthritis from the age of 19 and had been receiving cortisone 75 mg./day with good effect for the past fourteen months. For the previous few weeks she had noted a painless swelling of the left calf.

*On examination.*—Moderate rheumatoid involvement of most joints, not severe. No apparent effusion in left knee-joint. A large, tense, cystic swelling, which was only slightly tender and not hot, was present in the upper medial part of the calf. An X-ray of the knee-joint showed some secondary degenerative changes but no erosions. Chest X-ray normal. E.S.R. 33 mm. in one hour (Wintrobe). No L.E. cells were found. It was thought that she might have developed a tuberculous abscess and that drainage was indicated.

On incising the deep fascia, clear fluid was found, but on deepening the incision caseous material in large amounts issued from a cavity extending up to the popliteal fossa and beneath the origin of gastrocnemius laterally and down to the mid-calf superficial to soleus. The cavity was curetted, filled with streptomycin and closed without drainage. The suspicion of tuberculosis was increased when the culture was found to be sterile and was only partially allayed when the biopsy report subsequently revealed necrotic debris, muscle and areas of fat necrosis, with no evidence of tuberculosis, and was said to favour rheumatoid arthritis.

The wound healed except for a small area at the lower end and she was discharged home. Within two weeks, however, this area broke down, the knee suddenly became painful, swollen and flexed. It was hot but not red. It was thought that there might have been a spread of tuberculosis to the knee-joint and she was readmitted. Marked quadriceps wasting soon followed. Aspiration of the knee-joint yielded a slightly turbid fluid with numerous red cells, and a few white cells, which was again sterile. The cortisone was reduced to 12.5 mg., she was given streptomycin and para-aminosalicylic acid (PAS) and her pyrexia of 100–101°F. gradually settled over three weeks. She was discharged after six weeks with the

knee in a divided plaster-of-Paris cylinder. Chemotherapy was stopped after three months and she has had no further trouble with her knee or calf, although a 5-degree flexion deformity has remained.

*Case II.*—Woman aged 55, seen April 1958. She had had severe rheumatoid arthritis for the past four years, treated for the last two years with cortisone. Four months previously she had had an attack of pain in the left leg which was diagnosed as "phlebitis", when she could not walk, and the leg had since remained painful. Two months before her admission she had had a gradually enlarging, tense and painful swelling of the calf.

*On admission.*—Both knees were warm and unstable, with small effusions, and flexion of the left was limited to 45 degrees. A swelling in a similar situation to that in the first patient was present in the calf (Fig. 1).



FIG. 1.—Rheumatoid cyst of calf arising by herniation from the knee joint.

Aspiration yielded first some cloudy turbid fluid, then clear and straw-coloured fluid, but the cyst appeared to be loculated.

The orthopaedic surgeon (Mr. P. H. Newman) thought the cyst was a Baker's cyst having had connexion with the joint originally, although this was not now demonstrable. Excision was advised. The superficial wall of the cyst was formed by aponeurotic

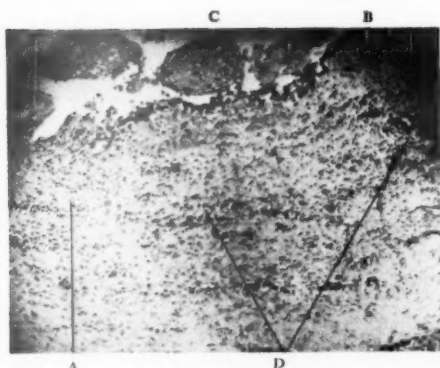


FIG. 2.—A, Increased fibrosis. B, Synovial cell proliferation. C, Fibrin body. D, Lymphocytic foci.

fibres of gastrocnemius with a thin lining of synovial membrane. Caseous material exuded from the cyst, which contained about 6 oz. (170 ml.) viscous yellow fluid. At the upper end there was a connexion with the medial side of the knee-joint, about the tendon of semi-tendinosus. As much as possible was excised and the whole painted with pure carbolic acid to try to prevent recurrence. A biopsy showed strips of tissue indistinguishable from synovial tissue in which there was increased fibrosis, synovial cell proliferation, fibrin bodies and lymphocytic foci, compatible with rheumatoid synovitis (Fig. 2).

The wound healed, but one month after discharge the cyst recurred. One month later there was again a tense fluctuant mass in the calf and this time the knee was considerably swollen. Injection of 50 mg. hydrocortisone into the knee-joint gave considerable relief and the calf swelling became less tense. She was given an elastic stocking. Now, six months later, there is no trace of the cyst and the knee is free from pain.

*Case III.*—Two months later, a man aged 52 was seen with a similar swelling in the right calf. He had suffered from rheumatoid arthritis since 1940, which had flared up and become generalized in 1948. He was not, however, having steroid therapy. The calf swelling had appeared two months before his admission and had become tense and brawny. He had suffered from pneumonia in 1930 and 1936, and had had a haemoptysis in 1953; X-ray of the chest at that time was considered to be typical of so-called rheumatoid lung. This was followed by two severe attacks of melena from a duodenal ulcer and he was actually admitted on the present occasion because of severe pain in the neck, followed by incipient quadriplegia. X-rays of the cervical spine showed the atlas dislocated forward on the axis and the odontoid peg could not be demonstrated. After neck traction by skull calipers, an arthrodesis was performed by Mr. Newman and he made a good recovery.

X-rays of his knee revealed erosive changes with a soft tissue swelling below the popliteal fossa (Fig. 3). Aspiration of the knee-joint yielded a sterile fluid

containing numerous polymorphonuclear leucocytes and mononuclear cells, with a moderate number of epithelial cells. Contrast medium was injected into the cyst, which was found to communicate with the joint (Fig. 4). It was not thought that surgery



FIG. 3.—Oblique radiograph of knee-joint showing a rheumatoid cyst of calf.

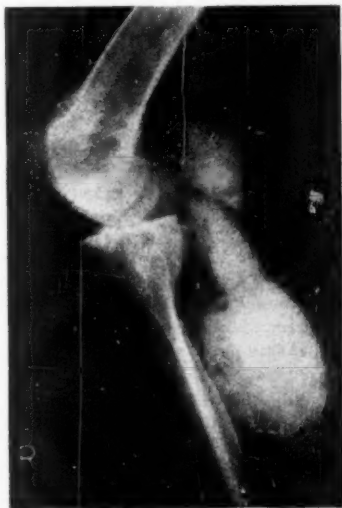


FIG. 4.—Injection of contrast medium into cyst, showing communication with knee-joint.

was indicated in view of his other disabilities. He has since left London and writes that the cyst has remained unchanged but is not painful.

Two further cases have been seen with similar swellings. The first was a man aged 49, who had had moderate rheumatoid arthritis for twelve years. He had latterly been treated with phenylbutazone. In May 1958 he had noticed a swelling of the right calf, which clinically communicated with the joint. By April 1959 the swelling was still hard, but he had no pain. Communication with the joint could not now be demonstrated.

The second case was of a man aged 51, who had had rheumatoid arthritis since 1947. The disease had been largely inactive recently. In June 1958 he developed a cold, painless swelling of the left calf. 10 oz. (285 ml.) of opalescent straw-coloured fluid was aspirated and 100 mg. hydrocortisone acetate instilled. Four weeks later the cyst had recurred and 200 mg. prednisolone trimethylacetate was injected. Since then there has been no recurrence.

These cysts seem to conform to the type first described by Baker in 1877 and 1885. He considered that a hernial protrusion of synovial membrane of a joint occurs through an aperture in its fibrous capsule, usually due to some chronic affection, especially osteoarthritis or tuberculosis, whereby intra-articular pressure is raised. These sacs contain synovial fluid and communicate at first with the joint. Later they burrow along muscle and fascial planes and appear at a distance from the joint, the aperture of communication with the joint having in some instances been shut off.

De Baets (1956) suggests that many so-called Baker's cysts actually have their origin in the bursae around the knee-joint. On the lateral side posteriorly that between the tendon of popliteus and the lateral femoral condyle and on the medial side that between the medial head of gastrocnemius and the capsule and semimembranosus usually communicate with the joint. Cysts of bursal origin probably account for those swellings seen in other situations round the knee-joint, such as the horse-shoe-shaped cyst described by Cameron and McGehee (1955).

Two examples were seen recently. The first probably arose from the semimembranosus bursa on the lateral side of the joint. The second (Fig. 5), also on the lateral side, may have arisen from the bursa between biceps femoris and the lateral ligament. This cyst was bilocular.



FIG. 5.—Rheumatoid cyst probably arising from bursa deep to tendon of biceps femoris.

Although I have not personally seen one, similar cysts occur in connexion with other joints and I have heard of one arising from the hip-joint like that described by Ferry (1955) and appearing in the femoral triangle and of one arising from the shoulder-joint, which was at first thought radiologically to be a sarcoma of the humerus.

From the point of view of treatment, these cysts are probably best left alone, with an elastic bandage as support. If painful, aspiration and instillation of hydrocortisone may be tried, but there is a tendency to rapid recurrence. If surgery is indicated, the cyst should be dissected out and the narrow neck which may lead to the joint closed. Even then, there is a considerable risk of recurrence.

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## The Injection of Concentrated Prednisolone Trimethylacetate Intra-articularly in Rheumatoid Arthritis

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*London*

THE injection of hydrocortisone into the finger-joints of patients suffering from rheumatoid arthritis usually results in both complete and lasting relief of pain, tenderness and swelling, but those same patients often derive a much less effective response, of much shorter duration, when their larger joints such as the knee are injected. The reason for this discrepancy may be that the dose of hydrocortisone used in the finger-joints is high when related to the size of the joint cavity and the surface area of the synovial lining. Pursuing this line of thought further led to a search for a more concentrated suspension of hydrocortisone, because to inject an adequate dosage of the ordinary concentrations of hydrocortisone at present available at 25 mg. to the ml. would mean injecting 10 to 20 ml. of fluid. Prednisolone trimethylacetate in a concentration of 200 mg. in 3 ml. appeared to be the answer to this problem and it is the results of a series of injections using this drug that is recorded.

The object of the trial was to answer the following questions. Could the concentrated steroid produce relief of pain, tenderness and swelling of much longer duration than that previously obtained, when the highest feasible dose of ordinary steroid had been injected? Could fluid be made to clear from a knee-joint without aspiration, by merely injecting a high enough dosage of steroid? Did any side-effects result from such high dosage therapy? The concentration of steroid used in this trial was that of 200 mg. in 3 ml. and, except in the first few injections, this was the dose used on each occasion, it being equivalent to approximately 500 mg. of hydrocortisone acetate in 20 ml. of fluid.

The method of injection was the same in all cases; either the normal anterior approach or, if aspiration was being carried out at the same time, the lateral patellar approach was used. No local anaesthetic was administered unless aspiration was attempted.

The patients all suffered from rheumatoid arthritis and had at least one knee-joint involved with a variable amount of fluid present. Cases with large effusions and with a previous history of resistance to hydrocortisone injection and aspiration were the most acceptable because it was felt that to obtain a response in these cases would mean that the conclusions might be significant. All the patients had had many previous injections of hydrocortisone up to a dosage of 100 mg. per

injection. The duration of response to these injections was known and from these records an average and best-ever response was calculated, the definition of response being relief of pain, decrease in tenderness, increased mobility and reduction in swelling. Most of the patients with large effusions had never been free from fluid for more than a few days after each aspiration for many months, and in one case quantities of up to 200 ml. of fluid were being removed at fortnightly intervals.

The patients in this trial all knew that they were being given a new highly concentrated form of hydrocortisone, as it was felt that it was more important to be able to record the observations of the patients as to any untoward reactions resulting from the injection than to conduct the trial to the satisfaction of the statisticians. Objective and subjective observations were made, the objective measurements were designed to give the greatest amount of information with the minimum of trouble both to the patient and to the flow of patients through a busy injection clinic. The measurements were made as far as possible at weekly intervals after the first injection and they were followed for many months afterwards; they included the diameter of the knee-joint measured at its widest part, to give a fairly accurate estimate as to the amount of fluid present. The distance between the mid-points of the lateral malleolus and the greater trochanter of the femur gave an idea of the amount of flexion possible, and the degree of tenderness was measured in the usual way by judging the reaction to finger pressure. Each patient was questioned with regard to the presence of indigestion or any relief of symptoms in joints other than the one injected, the presence of elation or depression, or the occurrence of pain at the time of, or soon after the injection; and the urine was tested for sugar at every visit. It was not felt necessary to estimate circulating eosinophils or urinary 17-ketosteroid excretion because Norcross (1958) has already demonstrated that the eosinophils fall and the 17-ketosteroid excretion is increased after the injection of large doses of hydrocortisone intra-articularly. After each injection patients were advised to remain off their feet as much as possible for the rest of that day but no other restrictions were placed upon them, and those who had had an effusion aspirated were advised to wear a crepe knee bandage until their next visit.

### Results

In all, 80 injections were given into 25 different joints and involving 22 patients. The results fall into four groups:

(1) 24% of the patients required only one injection, the response being so good that further injections were not necessary. One patient in this group had had 6 previous injections of hydrocortisone and had obtained an average and best response of three weeks, yet twenty-four weeks after one injection of the concentrated steroid she was still improving and the amount of fluid was negligible. Another patient in this group only recorded a maximum response of 2 days to 100 mg. injections of hydrocortisone and after one injection of prednisolone trimethylacetate the effusion took 9 weeks to return to its previous dimensions, and tenderness remained absent at the end of that period.

(2) 36% required several injections and then, as the fluid did not reaccumulate and the pain and tenderness did not recur, no further injections were given. These patients have shown no reaccumulation of fluid since.

(3) 28% required repeated injection but the intensity and the duration of the response was so good that it seemed worth continuing the treatment to save more frequent visits to the clinic.

(4) 12% showed no better response to the concentrated steroid than to the ordinary hydrocortisone.

In all, therefore, 88% of the patients showed a worthwhile response.

In several cases effusions cleared with one or more injections of steroid without aspiration but a much better response was obtained if aspiration preceded injection. When the diameters of the joints were measured at the average time of response and a mean taken of all these measurements, it was found that without aspiration the mean decrease was 0.5 inches, but with aspiration and injection it was 1.5 inches.

### Duration of Response

Fig. 1 shows a comparison between the average duration of relief in each patient to hydrocortisone 25 mg. per ml. (in black) and to prednisolone trimethylacetate 200 mg. in 3 ml. (in white).

It shows a considerable increase in the duration of response when concentrated steroid is used; this increase is three times as great, the average being two weeks relief with hydrocortisone and 5.7 weeks response with prednisolone. If the best-ever responses are compared then the average difference is 5.7 weeks to nine weeks.

These figures compare favourably with those of Norcross who injected varying concentrations of hydrocortisone, up to 250 mg. per ml., into the knee-joints of 60 patients, of whom 11 had osteo-

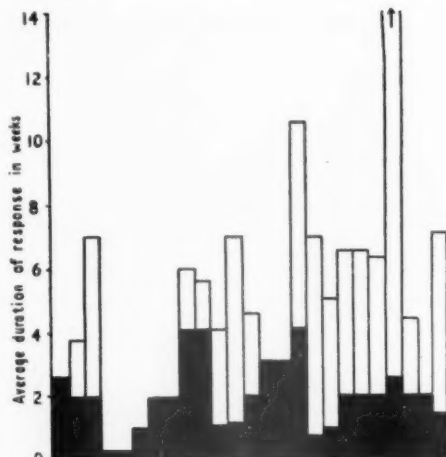


FIG. 1.

arthritis and 49 had rheumatoid arthritis. He found that the duration of response rose from six to thirty-four days.

The complications recorded after 80 injections were minimal. No patients showed glycosuria or mental depression. One patient had indigestion for twenty-four hours after the injection but not persisting. On 22 occasions the patients reported a generalized relief of symptoms in joints other than the one injected, lasting from one to seventeen days (nine days average), indicating some absorption of the steroid. One patient noted an excellent response in all joints for one week after injection, and this was followed by a generalized flare up. As this happened on two occasions it is fair to presume that he was having a withdrawal reaction to the large dose of steroid.

3 patients felt elated after the injection, but it is difficult to say whether this was a direct result of steroid absorption or due to the relief of joint pain. 4 patients complained of pain at the time of or soon after injection, but on no occasion did this alter the satisfactory response to the injection.

The results presented show that no greater risks arise from the use of high concentrations of steroid intra-articularly; a greater duration of response will result and effusions may clear without aspiration.

As Norcross suggests, it seems that the synovial lining of the larger joints such as the knee has a greater capacity than was previously believed to utilize a larger quantity of intra-articular steroid, so that a greater and more intense degree of improvement as well as increased duration of response will follow.

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## Rheumatoid Disease and Pneumoconiosis (Caplan's Syndrome)

By ANTHONY CAPLAN, M.D., M.R.C.P.

Cardiff

IN 1952 at a meeting of the Thoracic Society of Great Britain, attention was first drawn to an association in coal miners in South Wales of rheumatoid arthritis and certain unusual radiological appearances in chest radiograms (Caplan 1953). Epidemiological studies of rheumatoid arthritis in a community of coal miners in South Wales were carried out by the Pneumoconiosis Research Unit to investigate this syndrome (Miall *et al.*, 1953; Miall, 1955). The investigations confirmed the observation that a particular type of radiological appearance in the chest X-ray films of coal miners is closely associated with the presence of rheumatoid disease.

Examples of the syndrome have now been observed in coal workers in other parts of Great Britain and in other European countries (Christiaens *et al.*, 1954; Petry, 1954; van Mechelen, 1954; Dechoux and Ruysen, 1956; von Sepke, 1957), and in workers exposed to a variety of other dusts as in potteries, sand blasting, brass and iron foundries (Caplan, unpublished, 1954-1959; Caplan *et al.*, 1958); boiler scaling (Campbell, 1958); working with asbestos (Rickards and Barrett, 1958); and working in various silica hazards outside Britain (Colinet, 1950, 1953; Clerens, 1953; van der Meer, 1954; Martin and Fallet, 1953).

The radiological appearances are characterized by the presence of multiple, well-defined round opacities 0.5-5 cm. in diameter distributed throughout both lung fields (Fig. 1). In many cases the background of simple pneumoconiosis is slight or absent and the opacities often appear with a suddenness that is not usually observed in the development of progressive massive fibrosis (P.M.F.). Most frequently the development of the opacities coincides approximately with the onset of arthritis, but cases have been seen where the arthritis preceded the lung lesions up to periods of six years and in other cases the lung lesions have preceded the arthritis up to periods of ten years.

The tendency is for the opacities to increase in size and number, and crops of fresh lesions may appear at intervals of a few months. In a minority of cases a few round opacities are localized to one or more areas of the lung fields and may remain stationary. It is not uncommon for the lesions to cavitate, and when the cavitation is extensive the radiological appearances are quite striking and almost pathognomonic of the

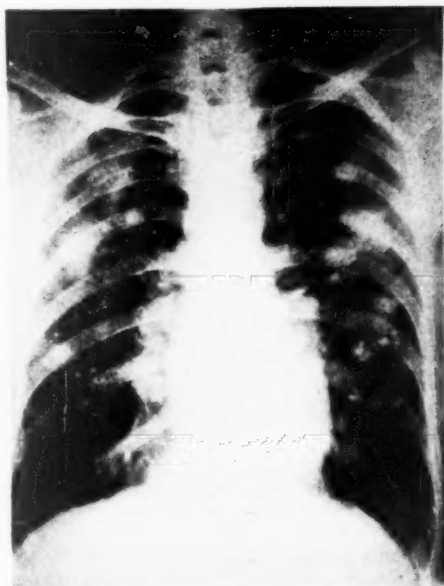


FIG. 1.—Characteristic radiological appearances of rheumatoid pneumoconiosis.

syndrome. Following cavitation the lesion may disappear completely or contract to a smaller irregular opacity. Calcification of the lesions is common. In many cases after a period of years the lesions become incorporated in a mass indistinguishable radiologically from P.M.F., although at post-mortem the conglomeration of multiple nodules is often recognizable. An uncommon complication is the development of a pleural effusion. More cases would probably be recognized if it were realized that the majority show a mixed radiological picture of round opacities and opacities indistinguishable from P.M.F.

There is no apparent relationship between the severity of arthritis and the extent and type of the X-ray picture. Cases of mild arthritis may be associated with a classical picture of many round opacities, but the chest X-ray film of a severely disabled arthritic miner may show very few opacities, or only slight or no apparent pneumoconiosis. A few cases with a characteristic chest X-ray picture have been observed to have typical



FIG. 2.—Large section of lung. The well-defined rheumatoid nodules (some cavitated) can be distinguished from the smaller irregular dust nodules.

olecranon nodules but no apparent joint changes.

A detailed pathological study of the syndrome has been made by Gough *et al.* (1955). They describe the lung lesions in 16 coal workers from material obtained at necropsy and biopsy as having a characteristic appearance and distinguishable from progressive massive fibrosis and the classical silicotic nodule (Fig. 2). Macroscopically the lesions show a characteristic concentric arrangement of lighter and darker layers. The pale areas are grey in some instances and yellow in others. Liquefaction tends to occur in the pale areas leaving clefts. In some cases the nodules are densely calcified.

Gough (Caplan *et al.*, 1958) suggests the histological criteria upon which diagnosis should be made are a central area of necrotic collagen, outside which is a zone of active inflammation consisting of a cellular infiltration of macrophages and frequently also of polymorphonuclear leucocytes. In this zone collagen is being destroyed. In hæmatoxylin-and-eosin-stained sections the intense blue staining of the inflammatory zone contrasts with the pink of the central necrotic collagen. Some of the macrophages in the inflammatory zone contain dust. When these macrophages die and disintegrate the dust is deposited and this accounts for the dark concentric rings seen in the nodules. The in-

flammatory zone may involve the whole or only part of the circumference of a nodule. Multi-nucleated giant cells are present in some instances, and these lie in a zone of fibroblasts outside the zone of inflammatory cells. The fibroblasts are orientated in a palisade manner. Outside the palisade is a zone of collagen arranged circumferentially and not necrotic. Endarteritis is present in vessels at the periphery of the nodules, and in the lumen of the vessels there are more lymphocytes and plasma cells than seen in the endarteritis usually present in pneumoconiosis.

In the first epidemiological study undertaken by the Pneumoconiosis Research Unit, it was observed that there was an increased prevalence of rheumatoid arthritis amongst men with P.M.F. A further survey of rheumatoid arthritis amongst males living in a Welsh mining valley was, therefore, carried out by Miall (1955) to study the relationship between rheumatoid arthritis and pulmonary abnormalities, particularly with reference to the possibility of massive fibrosis being responsible for the high incidence of rheumatoid arthritis in miners with complicated pneumoconiosis. Miall found no increased prevalence of rheumatoid arthritis amongst miners and ex-miners in a community where P.M.F. and cases of the rheumatoid syndrome were prevalent. He therefore concluded that neither exposure to dust nor the lung changes of complicated pneumoconiosis were of any importance in the aetiology of rheumatoid arthritis. There were, however, significantly high prevalence rates of P.M.F. and tuberculosis amongst miners and ex-miners with rheumatoid arthritis and of tuberculosis amongst non-miners with rheumatoid arthritis. Miall also made the interesting observation that in miners with a typical rheumatoid type chest X-ray appearance but without arthritis there was a familial incidence of rheumatoid arthritis similar to that found in cases of rheumatoid arthritis.

The symptomatology is similar to that found in massive fibrosis although there is in certain cases a surprising absence of constitutional disturbances and only slight impairment of respiratory function even when the chest X-rays show widespread opacities. This is perhaps even more striking in cases showing extensive cavitation. In 2 out of 50 miners with the syndrome who were fully investigated as in-patients, tubercle bacilli were found in the sputum. Even when extensive cavitation is present, a positive sputum is rare. This may indicate that the cavitation is not necessarily due to the breaking down of a caseating tuberculous focus, but to necrosis of collagen, the cause of which is so far unknown. It is, therefore, suggested that when cavitation occurs in rheumatoid lung lesions, a diagnosis of

active tuberculosis should await bacteriological proof. Persistent efforts should be made to isolate the tubercle bacillus, but if these prove negative, the case should be kept under observation rather than notified as tuberculosis. Treatment if indicated should be domiciliary rather than in a sanatorium. These suggestions are made because a number of such cases have been diagnosed as suffering from tuberculosis and subjected to a prolonged stay in sanatoria despite numerous negative sputum reports.

A wider recognition of the syndrome may also prevent an unnecessary diagnostic exploratory thoracotomy, for such procedures have been carried out in order to elucidate the pathology of round lesions in chest radiograms of coal workers suffering from rheumatoid arthritis. In these cases a provisional diagnosis of secondary tumour deposits or histoplasmosis was made.

The results of treatment of the lung lesions—as distinct from the arthritis—have been disappointing. On the assumption that the tubercle bacillus was a possible aetiological factor in the causation of the lung lesions, prolonged anti-tuberculous chemotherapy was given, particularly in cases showing a rapid increase in size and numbers of opacities and/or cavitation. In no case was there any obvious benefit. Corticosteroid therapy—sometimes combined with anti-tuberculous chemotherapy—has also had no effect on the progression of the lung lesions, except perhaps in one case which showed an apparent decrease in size of some of the radiological opacities after a twelve months' course of ACTH.

The aetiology of the lung lesions remains obscure. The lesions in coal workers and in workers exposed to a variety of dust hazards are histologically identical, a predominant feature being collagen necrosis. This suggests that a necessary factor in the aetiology of the lesion is the presence of collagen formed either as the result of the reaction to dust or to dust and tuberculosis.

It is possible that in subjects with rheumatoid disease this reaction is abnormal. The collagen necrosis may be either the cause or result of the abnormal response.

For many years it has been generally accepted that silicosis was due to the toxic effects of silica particles going slowly into solution; this chemical theory has now been discarded. The latest hypothesis is that an antigen-antibody reaction plays a part in the genesis of the silicotic nodule, the antigen being silica plus adsorbed body protein. It is known that in rheumatoid disease an abnormal agglutination factor may be present in the blood. It is possible that an antigen-antibody reaction also plays a part in the aetiology of the rheumatoid lung lesion in workers exposed to a dust hazard.

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#### Meeting

June 12–13, 1959

#### MEETING HELD AT CARDIFF

The following papers were read:

*At the Abbey Works of the Steel Company of Wales, Port Talbot*

**The Advantages of Early Diagnosis and Treatment in Industrial Injuries.**—Dr. RICHARD B. BODY.

*At the Royal Infirmary, Cardiff*

**The Demonstration of Joint Hernia in Rheumatoid Disease.**—Dr. J. A. B. JONES.

**Recovery in Bell's Palsy.**—Dr. KENNETH LLOYD.  
**Deformities in Children which Correct Themselves.**—Mr. DILLWYN EVANS.

**Pathological Changes in the Lungs in the Collagen Diseases.**—Professor JETHRO GOUGH.

**The Significance of Proteinuria in Rheumatoid Disease.**—Dr. B. McCONKEY.

**A Pilot Trial of Plaquenil in Rheumatoid Disease.**—Dr. I. A. WILLIAMS.

**Radiological Investigations in Paretic Disorders.**—Dr. A. S. BLIGH.

Cases and Demonstrations were presented by Members of the Medical Staff of the Royal Infirmary.

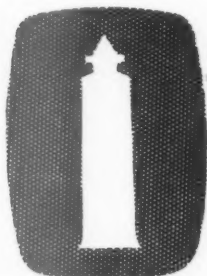
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# BOOK REVIEWS

**Das Röntgenschnittbild des Ohres: The Tomogram of the Ear.** By Professor Dr. Karl Mündnich and Dr. Kurt-Walter Frey. (In English and German. Pp. xii+123; 205 illustrations. DM 66) Stuttgart: Georg Thieme Verlag. 1959.

The reviewer is an otolaryngologist and not a radiologist. He found this a fascinating book. It has 205 illustrations, each one having a line drawing alongside interpreting the radiographs. The text is in two columns, the left being in German, and the right being an excellent English translation by Dr. F. Starer. It is probably fair to say that tomograms are difficult for the clinician to interpret, indeed the temporal bone is a very difficult anatomical region. Even a clinician can see the anatomical and pathological details demonstrated by the tomograms in this book after careful study of the line drawings. This diagnostic technique is not generally available in the major hospitals of the world, but it would obviously be desirable for any otologist to have this diagnostic aid available in difficult cases. The location of metallic foreign bodies in the temporal bone is apparently extremely accurate with this radiological technique. The anatomical detail convincingly demonstrated in these films is extraordinary. It is clearly not a technique to be used in routine radiology of temporal bones, but it is equally clear that in difficult clinical problems it would be an invaluable aid to the surgeon. An example is in congenital atresia of the external auditory meatus with a poorly pneumatized mastoid. These are frightening cases for the surgeon and pre-operative demonstration of the course of the facial nerve would remove many of the terrors of surgery.

The publishers are to be congratulated on the excellence of the reproduction of the radiographs and for arranging a key to the line drawings on a double page so that it is available for reference without turning pages.

**Medical Aspects of Flight Safety (The Unexplained Aircraft Accident).** Edited by E. Evrard, P. Bergeret and P. M. van Wulfpen Palthe. (Pp. ix+308; illustrated. 80s.) Published for Advisory Group for Aeronautical Research and Development, N.A.T.O. London: Pergamon Press. 1959.

Co-ordination of all research in the field of flight safety has become a major undertaking within the framework of N.A.T.O., and the task is entrusted to the Advisory Group on Aircraft Research and Development (A.G.A.R.D.). This

book is one of a series of AGARDographs covering the work and views of the various workers, as presented in papers at the Conferences held by A.G.A.R.D. As such, this work is a valuable addition to any reference library, and any research worker in this field would find it invaluable.

Though not claiming to be a textbook on flight safety, or indeed any particular portion thereof, the authors include many internationally recognized experts in their own field. Names like Franks, a pioneer in the acceleration field, now proving equally adept in metabolic variations as causes of unexplained aircraft accidents; Evrard, Graybiel, Melvill-Jones, to mention but a few of the familiar names working in disorientation—perhaps the biggest single problem confronting both military and civilian pilots to-day. In the extremist line, Colonel Stapp stands alone with his limit-probing adventures on his rocket sledge, revealing the acceleration limitations for the body in crashes as well as escapes from doomed aircraft.

In the more clinical role, once more Graybiel, Luehrs and Tompkins apply clinical acumen in assessing pilots' abilities, and fitness to fly.

Mason, a pioneer in the field of a specialized form of pathology, as applied to solving the cause of aircraft crashes, remains supreme as an individual. However, Townsend, in America, is able to introduce the statistical significance of pathological investigations in this important field.

**Notable Names in Medicine and Surgery.** By Hamilton Bailey, F.R.C.S.(Eng.), F.A.C.S., F.R.S.(Edin.), and W. J. Bishop, F.L.A. 3rd ed. (Pp. xiii+216; illustrated. £1 15s.) London: H. K. Lewis & Co. Ltd. 1959.

Reviewers, like many a "gentle reader", apparently recoil from reading any form of Preface. The authors of this most attractive and interesting book have therefore been obliged to take measures to overcome this aversion by inserting an Introduction, boldly outlined in scarlet, wherein is stated the precise purpose of the publication, a point on which they had suffered some criticism in the past. It is generously implied that qualified medical men are already fully acquainted with the information set out in the following pages, the perusal of which is recommended to students and non-medical personnel in hospitals, dispensaries, drug firms and similar institutions. Here the use of eponymous terms is a daily occurrence and remarks such as "Who was Glauber, or is it a place?" must often be

made. It is to answer these questions that the book was written.

This new edition not only contains more pages but the pages themselves are larger. The quality of the illustrations is markedly improved and once again colour is used, sparingly but with good effect. The addition of footnotes will be appreciated by those who like their knowledge precise.

The authors are to be congratulated on the high standard of interest and information that has been maintained. Those who have enjoyed reading the two previous editions will find pleasure in renewing acquaintance with old friends and in being introduced to new ones, while the new reader can look forward to a delightful excursion into the lighter side of medical history.

**Diseases of Metabolism. Detailed Methods of Diagnosis and Treatment.** Edited by Garfield G. Duncan, M.D. 4th ed. (Pp. xxii + 1104; illustrated. £6 9s. 6d.) Philadelphia and London: W. B. Saunders Company. 1959.

In the seven years that have elapsed since the third edition of this book was printed, metabolic diseases have been the subject of intensive investigation. The advances achieved have been ably incorporated in this current edition, and for a text of this great size the information is admirably up to date. The choice of subjects is somewhat arbitrary and includes diseases of the thyroid gland and the kidneys in addition to more purely metabolic disorders such as gout, glycogen storage disease and water balance. Being of multiple authorship the chapters differ somewhat in the emphasis given to biochemical and clinical aspects, but this does not detract from the enthusiasm with which each topic is tackled. The concept of the book is encyclopædic so that it is an excellent work of reference and of value to the expert or clinical investigator; but the ordinary student or practitioner may find it rather too detailed for his needs. Some idea of the size of the work is given by the fact that the chapter on thyroid diseases has more than 800 references.

**International Textbook of Allergy.** Editor: J. M. Jamar, M.D. (Pp. 639; illustrated. £5 10s.) Oxford: Blackwell Scientific Publications. 1959.

This book covers the growing field of allergy in a comprehensive manner and the contributors include well-known authorities from most countries in Europe and from the North and South American continents.

The first section is concerned with modern views on the mechanism of anaphylaxis (Roche

E. Silva), the role of histamine in man (J. Lecomte) and the immunological approach to allergy (K. Sherwood Lawrence).

The remainder of the book is concerned mainly with the clinical aspects of allergic disease, and includes articles on the prevalence, diagnosis and treatment of asthma and rhinitis. Treatment is discussed under a variety of headings including desensitization, non-specific therapy, antihistamines, treatment of status asthmaticus and the use of steroids in asthma. There is a thorough review of the importance of emotional factors in allergic disease. Other points discussed are the problem of allergy in relation to diseases of the skin, the cardiovascular system, the eye, the blood-forming tissues and the collagenoses.

It would be invidious to discuss the contributions of individual authors when the level throughout is so high: some of the chapters dealing with complex phenomena are indeed models of clarity and brevity. When it is appreciated that the entire work is published in English, a language with which many of the contributors are only imperfectly acquainted, it is evident that the editor deserves unqualified congratulations.

The book can be strongly recommended not only to allergists, but to all those who wish to understand more of the basic principles underlying the modern conception of allergic disease and the practical measures adopted for dealing with it.

**The Child with a Handicap. A Team Approach to His Care and Guidance.** Edited by Edgar E. Martner, M.D. (Pp. xxiv + 409; illustrated. 82s. 6d.) Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

The handicapped child has become the focus of considerable interest and activity in recent years and in this country a number of organizations have come into being to further the interest of these children and their parents. This book reflects this growing interest. It sets out to provide a team approach to the care and guidance of the child with a handicap by compiling the individual contributions of some 27 specialists. The table of contents looks most inviting for nothing appears to have been omitted—"comprehensive" is the keynote. Although some of the individual sections are excellent and for the American consumer there are some valuable compiled lists of agencies and sources of material, the book as a whole fails to come up to expectation due to a lack of cohesion. The standard varies from erudite focal points raised by recent research to view-points of naïve simplicity. What is mainly lacking is the variety of everyday human

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problems that a given handicap raises for the child, the parent and the physician and how such problems need to be tackled in workaday detail.

**Essential Principles of Pathology.** By John W. Landells, M.A., M.B., M.R.C.P., F.Z.S. (Pp. x+278; illustrated. 25s.) London: Pitman Medical Publishing Co., Ltd. 1959.

This book is written for the student who has just arrived on the wards. It provides a brief and comprehensive introduction to pathology, and has excellent references for the further reading of any particular topic.

When giving a student his basic knowledge it is essential to be clear and accurate; the author comes well up to these standards. He is a morbid anatomist, and the sections which are primarily morbid anatomy are excellent. For further reading in bacteriology, one is referred to the companion volume which is soon to be published.

The book is easy to read and up to date with sections on radiation and auto-immune disease. The section on anaemia is inadequate and there are one or two incorrect inferences, namely that brucellosis can cause abortion in humans, and that staphylococcal food poisoning can occur by means other than toxic.

The illustrations consist entirely of monochrome photomicrographs, which may seem puzzling to the new student. This is done to make the book compact and economical. The price is one that any student can readily afford.

**Zur Orthologie und Pathologie der Hoyer-Grosser'schen Organe.** By Dr. med. Julius Schorn. No. 6 of *Zwangslose Abhandlungen aus dem Gebiet der normalen und pathologischen Anatomie*. (Pp. 88; 46 illustrations. DM 27.50). Stuttgart: Georg Thieme Verlag. 1959.

This monograph in Bargmann and Doerr's series records observations on the arteriovenous anastomoses ("Hoyer-Grosser organs") in the extremities of the limbs in normal persons and in patients who had died from various diseases—among them essential and renal hypertension—in which changes in small distal blood vessels seemed likely to be present. The author gives full details of his normal and morbid histological findings—obtained from serial sections of specimens removed from 44 subjects—and illustrates his text with numerous excellent photomicrographs. This study was pursued along almost wholly morphological lines, and the observations set down are likely to prove of most value to those interested in the peripheral vascular changes in hypertensive diseases.

**Somatic Complications following Legal Abortion.**

By Jan Lindahl. Translated by S. H. Vernon. (Pp. 182. 42s.) Stockholm: Scandinavian University Press. London: William Heinemann Medical Books Ltd. 1959.

This book is translated from the Swedish and is a careful follow-up of legal abortion in Sweden. It must be pointed out that termination of pregnancy has been legal in that country since 1938.

This is probably a unique study and therefore will be of particular interest to gynaecologists.

Well over a thousand cases are reviewed and it should be noted that there was one death from intraperitoneal haemorrhage. The most important post-operative complication was endometriosis which is specially liable to occur in patients who have had vaginal hysterotomy.

Fertility was not impaired except in 5 patients with salpingitis. Functional symptoms were frequent but not attributable to physical effects of the operation.

The author is to be congratulated on his conscientious follow-up of this series of cases.

**The Sudan Medical Service. An Experiment in Social Medicine.** By H. C. Squires, C.M.G., D.M., F.R.C.P., D.P.H. (Pp. xii+138; 7 illustrations. 15s.) London: William Heinemann Medical Books Ltd. 1958.

The compilation of this book has evidently been a labour of love for Dr. Squires. The Sudan Medical Service was inaugurated in 1904, Dr. Squires joined it in 1908 and was associated with it for the next forty-three years. To some extent his book resembles a regimental history, with every possible name and deed recorded, and a systematic account given of the progress of medical and nursing education, &c. But the Sudan, extending almost from the equator to the tropic of Cancer, contains every type of country and climate to be found in northern Africa, and its people suffer from the diseases typical of such climates on a scale unsurpassed anywhere. As a result, it is the most fully equipped epidemiological museum in the world. What does a doctor actually do when he finds himself single-handed in an almost roadless area of several thousand square miles, in which some hundreds of persons are succumbing daily to an epidemic disease? Dr. Squires gives a glimpse of how epidemics can be tackled successfully in such circumstances, and one would have welcomed more of these front-line accounts. But that must wait until one of the front-line doctors themselves, Bryant, Corkill, Kirk and others, takes up an autobiographical pen. Meanwhile, here is a very

readable and interesting book, which fills in part of the human medical background of the wide canvas of Brockington's "World Health".

**The Cranial Nerves.** By Alf Brodal, M.D. Translated from the Norwegian by the author. (Pp. 141; 25 illustrations. 15s.) Oxford: Blackwell Scientific Publications. 1959.

This pocket-size book with its pleasant, green, stiff-paper binding looks most inviting. It seems almost to promise light reading and although "light" is not the right word it is certainly easy to read because it never fails to interest. Remembering Professor Brodal's other writings on neuro-anatomy this is what one would expect. The smallness of the volume is encouraging and the reading of it gives a sense of achievement.

After a brief review of some general features of the cranial nerves giving something of a bird's eye view, the author writes about each cranial nerve in turn beginning from below upwards. He describes first the anatomy in considerable detail and with adequate diagrams; then comes an outline of function and finally a note of the salient clinical features in disorders of each nerve. Of these three aspects the anatomical is treated in greatest and the clinical aspect in least detail which, of course, is the soundest balance to strike in a book of this kind. It should be welcomed by all trainees in neurology, particularly in their postgraduate studies, and it can be most warmly recommended.

Is it too much to ask of anatomy books in general that when reference is made to a diagram its page should be given as well as its number?

**Sympathectomy. An Anatomical and Physiological Study with Clinical Applications.** By P. A. G. Monro, M.A., M.D.(Cantab.), M.Sc.(London). (Pp. xx+290; illustrated. 75s.) London: Oxford University Press. 1959.

This book embodies the work of an anatomist who has worked with the Neurosurgical Unit of the London Hospital to study the effects of sympathectomies in patients over a number of years. The sweating patterns and vasomotor changes have been studied in particular and the author describes the apparatus and methods used.

In addition to reporting his own findings, he has reviewed the work done by others in his particular fields of interest. He has produced up-to-date summaries and conclusions on such problems

as gustatory sweating, the late results of sympathectomies for hypertension, and the causes of return of vasomotor nervous activity in the upper limb after upper dorsal sympathectomy.

Some anatomical or physiological aspects, such as operations on the sympathetic afferent fibres for relief of cardiac or other pain, are less fully covered.

This is not a practical guide for surgeons but can be strongly recommended for reference and enlightenment to anyone interested in the anatomy and physiology of the autonomic nervous system and its role in health and disease.

**A Color Atlas of Morphologic Hematology.** By Geneva A. Daland, B.S. Edited by Thomas Hale Ham, M.D. Revised edition. (Pp. 72; illustrated, with 16 colour plates. 55s.) Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1959.

This new edition is beautifully produced and sets out to be a reference guide for the study of peripheral blood films stained by Wright's stain. The basis of the work consists of 16 art plates, most of them showing two films, with accompanying outline drawings and keys. The 58-page text gives short descriptions of technique, of normal and pathological blood cells, and of the diseases illustrated, with detailed description of the plates. Bone-marrow findings are not depicted.

This book is more suited for beginners and technicians than experienced haematologists. Within its chosen limits the text is excellent and well judged, even if the rather extensive bibliography seems largely unnecessary in a book of this type. The reviewer is not, however, as happy about the plates. They are reproductions of paintings (by Etta Piotti) and, however carefully done, paintings are not quite the same as the real thing. A more serious criticism is that the plates show idealized blood pictures. The cells from several fields have been brought together and although this may make the pictures more dramatic and interesting they become more and more unreal and exceptional. The reviewer also finds it impossible not to quarrel with the selection of plates. Why, for instance, do we have two pictures of plasma-cell leukaemia and none of acute myeloblastic leukaemia? It seems a pity, too, that the plates are placed at the end of the work. Their natural place is adjacent to the corresponding text. As it is, it seems likely that the plates will be looked at and the excellent text mostly left unread.

- \* "The noses of healthy individuals probably form by far the largest breeding ground for the pathogenic staphylococci . . . ."

Brit. Med. J. ii, 658, Oct. 10th 1959

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#### Reference Lancet, 1957, ii, 1157

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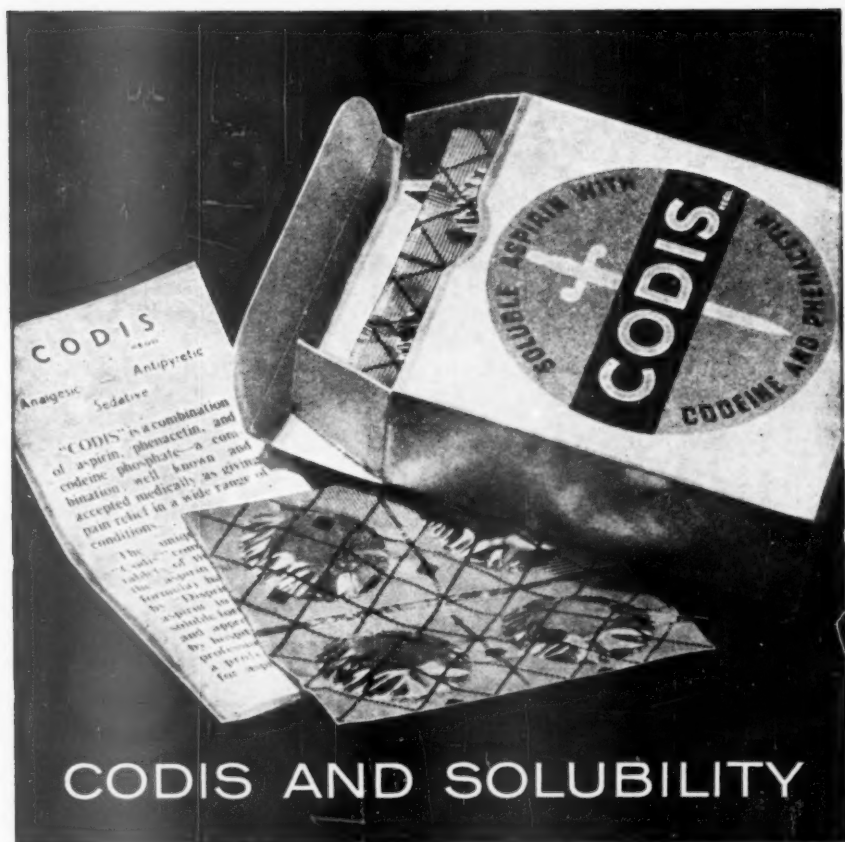


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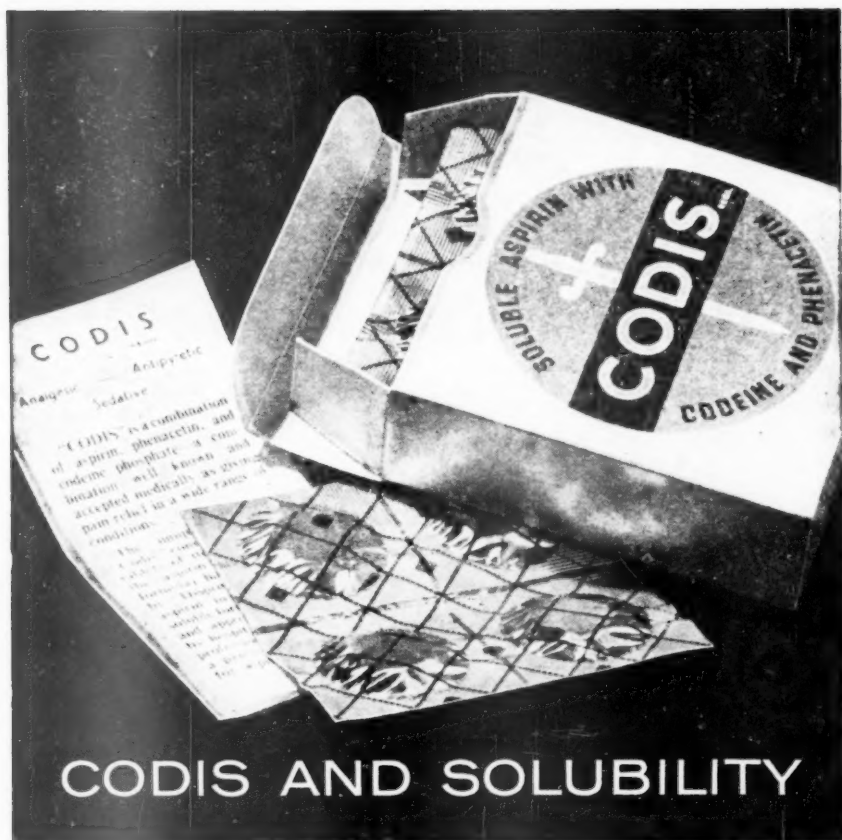
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